WEST Search History

AH# 11

DATE: Wednesday, August 28, 2002

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DB = USPT, P			
L18	11 same 18	8	L18
L17	11 with 18	3	L17
L16	110 with L5	13	L16
L15	110 wiht L5	0	L15
L14	110 and L5	212	L14
L13	11 same 15	1	L13
L12	11 with 15	1	L12
L11	11 and L10	1	L11
L10	organ preservation	554	L10
L9	11 and 15 and L8	103	L9
L8	cell or cellular or tissue	1138401	L8
L7	11 and L5	315	L7
L6	11 and 14	72	L6
L5	freez\$ or frozen	230572	L5
L4	cryo\$	53450	L4
L3	11 and L2	4	L3
L2	cryopreserv\$ or cryoprotect\$	3434	L2
L1	cyclohexanediol	4642	Ll

END OF SEARCH HISTORY

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1. 20020068360. 17 Apr 01. 06 Jun 02. Cyclohexanediol cryoprotectant compounds. Brockbank, Kelvin G.M., et al. 435/374; C12N005/00.				
2. 6008417. 07 Oct 98; 28 Dec 99. Process for making metabolites of lycopene. Pfander; Hanspeter, et al. 568/838;. C07C035/06.				
3. <u>H001093</u> . 08 Jan 90; 04 Aug 92. HCL monitoring apparatus and method for process gas streams. Huston; Gregg C 436/101; 422/62 422/88 422/90 436/121 436/122 436/123. G01N033/00 G01N021/00 G01N030/96.				
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6. 4094869. 16 Jun 75; 13 Jun 78. Thermally stable, rigid, cellular isocyanurate polyurethane foams. Biranowski; Jerome B., et al. 521/118; 521/123 521/171 521/902. C08G018/14.				
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- 1. 20020068360. 17 Apr 01. 06 Jun 02. Cyclohexanediol cryoprotectant compounds. Brockbank, Kelvin G.M., et al. 435/374; C12N005/00.
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96. 4033911. 24 Jun 76; 05 Jul 77. Process for catalyzing polyurethane foam formation using N,N-dimethyl-aminoalkoxy-propionitriles. Sandner; Michael Ray, et al. 521/129; 521/127 521/174 528/76. C08G018/14.					
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99. <u>3871885</u> . 20 Oct 72; 18 Mar 75. CRYSTALLINE PHOTO-POLYMERIZABLE COMPOSITION. Hertler; Walter Raymond. 430/281.1; 430/271.1 430/283.1 430/916 430/923 522/37 522/39 522/40 522/43 522/46 522/6 522/63 522/9. G03c001/68 G03c001/70.					
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☐ 102. <u>3644168</u>. 12 Jun 70; 22 Feb 72. VARIED DENSITY POLYISOCYANURATE FOAM STRUCTURE. Bonk; Henry W., et al. 442/213; 264/41 264/45.3 264/45.5 264/46.7 273/DIG.8 428/116 428/315.7 428/318.8 428/422.8 428/73 473/120 473/567 521/114 521/134 521/156 521/51. B32b003/26 B32b005/14 B29d027/00.

☐ 103. <u>US 20020068360 A1 WO 200178505 A1 AU 200155433 A</u>. Cryopreservation of <u>cells</u> involves contacting <u>cells with cyclohexanediol</u> compound, and subsequently reducing the temperature of <u>cells</u> to cryopreservation temperature. BROCKBANK, K G M, et al. A01N001/02 C12N005/00.

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=> s 13cyclohexanediol and 14cyclohexanediol AU 2001055433 A AU 2001-55433 20010417 0 13CYCLOHEXANEDIOL AND 14CYCLOHEXANEDIOL US 2002068360 A1 Provisional US 2000-197669P 20000417 L1 US 2001-835818 20010417 => s cyclohexanediol FILING DETAILS: 2514 CYCLOHEXANEDIOL PATENT NO KIND PATENT NO => s "1,3" 4 FILES SEARCHED... L3 1847673 "1,3" AU 2001055433 A Based on WO 200178505 PRIORITY APPLN. INFO: US 2000-197669P 20000417; US 2001-835818 => s"1.4"20010417 4 FILES SEARCHED... AN 2002-089629 [12] WPIDS AB WO 200178505 A UPAB: 20020221 L4 1415573 "1,4" NOVELTY - Cells are ***cryopreserved*** by contacting the cells => s 13 and 14 ***cryopreservation*** composition containing ***cyclohexanediol*** L5 162390 L3 AND L4 (CHD) compound, and subsequently reducing the temperature of the cells => s 12 and 15 a ***cryopreservation*** temperature. 444 L2 AND L5 USE - For ***cryopreservation*** of cells. L6 ADVANTAGE - The method increases cell viability upon warming => s freez? or preserv? or cryo? from a L7 846158 FREEZ? OR PRESERV? OR CRYO? frozen state. Dwg.0/5 => s 16 and 17 L9 ANSWER 2 OF 3 WPIDS (C) 2002 THOMSON DERWENT 5 L6 AND L7 L8 DUPLICATE 2 ACCESSION NUMBER: 2000-317282 [27] WPIDS CROSS REFERENCE: 2000-303114 [24] => dup rem 18 PROCESSING COMPLETED FOR L8 3 DUP REM L8 (2 DUPLICATES REMOVED) DOC. NO. CPI: C2000-095882 New ***cryopreservative*** solutions, useful for TITLE: ***preserving*** biological samples such as cells, => s 19 ibib abs 1-3 embryos, tissues, organs and animals. MISSING OPERATOR L9 IBIB DERWENT CLASS: A96 B04 D16 D22 The search profile that was entered contains terms or INVENTOR(S): FAHY, G M; WOWK, B nested terms that are not separated by a logical operator. PATENT ASSIGNEE(S): (TWOO-N) 21ST CENTURY MEDICINE INC; => d 19 ibib abs 1-3 (FAHY-I) FAHY G M; (WOWK-I) WOWK B L9 ANSWER 1 OF 3 WPIDS (C) 2002 THOMSON DERWENT COUNTRY COUNT: DUPLICATE 1 PATENT INFORMATION: ACCESSION NUMBER: 2002-089629 [12] WPIDS DOC. NO. CPI: C2002-027553 PATENT NO KIND DATE WEEK LA PG ***Cryopreservation*** of cells involves contacting TITLE: cells with ***cyclohexanediol*** compound, and WO 2000016618 A1 20000330 (200027)* EN 46 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE subsequently reducing the temperature of cells to ***cryopreservation*** temperature. LS LU MC MW NL DERWENT CLASS: B04 D22 E15 OA PT SD SE SL SZ TZ UG ZW INVENTOR(S): BROCKBANK, K G M; CAMPBELL, L H; W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU TAYLOR, M J CZ DE DK DM EE ES PATENT ASSIGNEE(S): (ORGA-N) ORGAN RECOVERY SYSTEMS FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ INC; (BROC-I) BROCKBANK K LC LK LR LS G M; (CAMP-I) CAMPBELL L H; (TAYL-I) TAYLOR M J LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD COUNTRY COUNT: SE SG SI SK SL TJ PATENT INFORMATION: TM TR TT TZ UA UG UZ VN YU ZA ZW AU 2000010939 A 20000410 (200035) PATENT NO KIND DATE WEEK LA PG EP 1115281 A1 20010718 (200142) EN R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV WO 2001078505 A1 20011025 (200212)* EN 20 MC MK NL RO RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE SI US 6395467 B1 20020528 (200243) LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN APPLICATION DETAILS: CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE PATENT NO KIND APPLICATION DATE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO WO 2000016618 A1 WO 1999-US21736 19990921 NZ PL PT RO RU SD AU 2000010939 A AU 2000-10939 19990921 SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW EP 1999-954636 19990921 EP 1115281 A1 WO 1999-US21736 19990921 AU 2001055433 A 20011030 (200219) US 2002068360 A1 20020606 (200241) US 6395467 B1 Provisional US 1998-101194P 19980921 Provisional US 1999-127158P 19990331 APPLICATION DETAILS: US 1999-128142P 19990407 Provisional

FILING DETAILS:

PATENT NO KIND

WO 2001078505 A1

APPLICATION DATE

WO 2001-US12465 20010417

Provisional

al US 1999-143587P 19990713 US 1999-400793 19990921 PATENT NO KIND

PATENT NO

AU 2000010939 A Based on EP 1115281 A1 Based on

WO 200016618 WO 200016618

PRIORITY APPLN. INFO: US 1999-143587P 19990713; US 1998-101194P

> 19980921; US 1999-127158P 19990331; US 1999-128142P 19990407; US 1999-400793 19990921

AN 2000-317282 [27] WPIDS

CR 2000-303114 [24]

AB WO 200016618 A UPAB: 20020709

NOVELTY - New ***cryopreservation*** solutions are obtained by changing the components of solutions and determining the effect on toxicity, vitrification and ability to resist devitrification.

DETAILED DESCRIPTION - A novel solution for

cryopreservation

of biological samples comprises at least one ***cryoprotective*** agent for which qv is between 1 and 2, where the total concentration of the ***cryoprotective*** agent is between 5 and 150 % of its Cv; and where the toxicity of the solution for ***cryopreservation*** causes at most 50% reduction in viability as measured in a kidney slice assay.

qv = the moles of water per mole of polar group at Cv;

Cv = the concentration needed to vitrify 5-10 ml of the solution at a cooling rate of 10 deg. C/minute.

INDEPENDENT CLAIMS are also included for:

(1) a method for producing optimal solutions for vitrification comprising: (a) selecting dimethylsulfoxide and formamide in a molar ratio of 1.1-0.8 and at a total concentration of 30-45% w/v; (b) selecting an additional penetrating ***cryoprotective*** whose qv is below 2; (c) adding the additional penetrating ***cryoprotective*** agent to the dimethylsulfoxide and formamide in varying concentrations; (d) cooling

resulting mixtures so as to determine the concentration of the additional ***cryoprotective*** agent to vitrify the solution; (e) subtracting 2-6% w/v of the additional ***cryoprotective*** agent; (f) replacing the 2-6% w/v of subtracted additional ***cryoprotective*** agent with

w/v non-penetrating agent; and (g) adding a fourth penetrating ***cryoprotective*** agent if the solution does not vitrify to restore the solution to its Cv; (h) exposing the biological system to the discovered vitrification solution with or without subsequent vitrification; and (i) testing the biological sample for viability;

- (2) a method for optimizing the ***freezing*** of biological systems comprising: (a) selecting an optimum vitrification solution as in (1); (b) exposing the biological system to a dilution of the vitrification solution yielding a final concentration of penetrating agent of 2-35% w/v, or of 0.2-4M; and (c) cooling the system;
- (3) a ***cryoprotectant*** solution comprising dimethyl sulfoxide, an amide or a combination of amides, and at least one penetrating ***cryoprotective*** chemical where the qv of the solution in aqueous solution is below 1.9 and where the toxicity of the solution at its qv is less than the toxicity of VS41A;
- (4) a ***cryoprotective*** solution comprising dimethyl sulfoxide and at least 2 penetrating ***cryoprotective*** chemicals where the qv values of the penetrating ***cryoprotective*** chemicals in aqueous solution are below 1.9 for each ***cryoprotective*** chemical, or where the vitrification to a cooling rate of approx, 30 deg. C/minute or less, and where the ***cryoprotective*** solution is less toxic than VS41A;
- (5) a vitrification solution comprising dimethyl sulfoxide, an amide or combination of amides, and at most 16% w/v 1,2-propanediol;

(6) a ***cryoprotectant*** solution having a qv of at most 1.9;

(7) a method of ***preserving*** a living system by supercooling, comprising: (a) distributing through the system a non-toxic amount of polyvinyl alcohol, at a concentration of 0.01-6% w/v, in combination with a concentration of ***cryoprotectant*** to allow supercooling of the living system at the desired storage temperature, which concentration of

cryoprotectant may range from 0-60% w/v, at a temperature

from -20 to 37 deg. C; (b) cooling the living system to the storage temperature, ranging from 0 to -100 deg. C; (c) storing the system; (d) warming the system back to -20 to 37 deg. C; and (e) removing the ****cryoprotectant*** and polyvinyl alcohol;

(8) a ***cryoprotectant*** solution comprising a concentration of

urea to eliminate devitrification at a warming rate of 70 deg. C/minute or less when the solution is at its Cv;

(9) a method for composing vitrification solutions containing non-penetrating high molecular weight polymers (over 11000 daltons in mass), comprising: (a) subtracting 1-7% of the penetrating

cryoprotectant that would otherwise be needed to vitrify; and (b) replacing this penetrating ***cryoprotectant*** with 2-8% w/v of the high molecular weight polymer;

(10) a method for selecting good candidate ***cryoprotectant*** solutions from poor candidate solutions comprising: (a) determining the total concentrations of the candidate solutions that are needed to vitrify; (b) determining the qv of the solutions; (c) ranking the solutions based on their qv values; and (d) preferentially testing solutions having the lower qv values.

USE - The solutions can be used for ***preserving*** biological samples, e.g. cells, embryos, tissues, organs or animals (claimed). They can also be used for the ***cryopreservation*** of proteins, organelles, cell extracts, blood vessels, artificial or engineered cells, tissues, blood vessels, organs or organoids, or other biological systems by vitrification, ***freezing*** or other means.

ADVANTAGE - The solutions can provide for ***cryoprotection*** while minimizing toxicity without weakening their ability to vitrify and to resist devitrification.

Dwg.0/10

L9 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS 1967:443383 HCAPLUS

ACCESSION NUMBER:

67:43383

DOCUMENT NUMBER: TITLE:

Synthesis of esters of .alpha.,.alpha.-dimethyl

alkanoic acids

Zharova, E. Ya.; Puzitskii, K. V.; Rapoport, I. B.; Eidus, Ya. T.; Velizar'eva, N. 1.

AUTHOR(S): SOURCE:

74-6.degree./10,

Neftekhimiya (1967), 7(1), 92-6

CODEN: NEFTAH

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Neo acids (.alpha.,.alpha.-dimethyl acids) were prepd. by carboxylation

olefins or monovalent said. alcs. with CO at 40.degree./30-50 atm. in the presence of H2SO4. Homologs C13 (b17 165-200.degree.) and C16 (b10 165-98.degree.) were prepd. from tetramers or pentamers of propylene.

acids were then converted to the corresponding acid chlorides in 80-90% yield by adding excess SO2Cl2 dropwise at 76-9.degree.. The prepd. neo acids have the following b.p./mm., d20, and n20D: C5, 47-9.degree./10, 0.9676, 1.4312; C8, 57-8.degree./10, 0.9571, 1.4349; C9,

0.9497, -; C10, 90-1.5.degree./10, 0.9435, 1.4422; C11, 125-6.degree./21, 0.9347, 1.4443. Alcs. were acylated with acid chlorides at 50-100.degree., HCl was removed at 100.degree. with N, the products

washed with NaOH and Na2CO3 solns., then with water, and fractionated.

The yields were 85-95% with respect to acid chloride and 70-90% with respect to neo acid. Crude ***1*** , ***3*** -

cyclohexanedio1 esters contain monoesters and 65% diesters. Monoesters, ***freezing*** between -63 and -49.degree., have the following b.p. at 1-2 mm., n20D, and viscosity at 50.degree. in centistokes: C7, 105-68.degree., 1.4539, 8.2; C8, 120-80.degree., 1.4572, 6.4; C9, 135-92.degree., 1.4612, -; C10, 137-98.degree., 1.4608, 10.2; C11, 106-209.degree., 1.4612, 10.0. Analogously, the same values of diesters ***freezing*** between -46 and -40.degree, are as follows: C7, 168-70.degree., 1.4535, 9.5; C8, 180-1.degree., 1.4549, 11.2; C9, 192-4.degree., 1.4579, 15.9; C10, 198-200.degree., 1.4587, 21.8; C11, 209-11.degree., 1.4600, 24.4. These characteristics are further given for the esters of neo acids and polyols: C8, (CH2)6(OH)2 178-80.degree., 1.4430, 7.0; C7, (CH2)10(OH)2 192-4.degree., 1.4452, 8.6; C8, (CH2)10(OH)2

202-5.degree., 1.4481, 10.0; C7, trimethylolpropane, 213-24.degree., 1.4490-1.4509, 18.9-22.9. Diol esters ***freeze*** at the temp. between -63 and -69.degree., the triol ester at -45.degree.. The esters of 2-ethyl-1-hexanol and neo acids (***freezing*** at -67.degree. or lower) have the following characteristics (ordered in the above sequence): C7, 112-14.degree., 1.4330, 2.0; C9, 114-16.degree., 1.4365, 2.4; C13, 154-60.degree., 1.4460, 5.7; C16, 156-66.degree., 1.4510, 7.0. Mixts. of esters of C7 neo acid and 2-ethyl-1-hexanol and ***1*** , ***3*** ***cyclohexanediol*** have improved phys. properties. Thus, the

of these esters in the ratio ***1*** : ***4*** ***freezes*** at -63.degree. and has visocisity 6.06 centistokes at 50.degree..

=> d his

(FILE 'HOME' ENTERED AT 12:33:13 ON 29 AUG 2002)

FILE 'BIOSIS, EMBASE, MEDLINE, WPIDS, HCAPLUS' ENTERED AT 12:33:22 ON 29

AUG 2002

0 S 13CYCLOHEXANEDIOL AND 14CYCLOHEXANEDIOL

L2 2514 S CYCLOHEXANEDIOL

1847673 S "1,3" L3

1415573 S "1.4" L4

1.5 162390 S L3 AND L4

444 S L2 AND L5

L7 846158 S FREEZ? OR PRESERV? OR CRYO?

5 S L6 AND L7

3 DUP REM L8 (2 DUPLICATES REMOVED)

=> s cell or cells or cellular or tissue?

2 FILES SEARCHED..

L10 11943103 CELL OR CELLS OR CELLULAR OR TISSUE?

=> s 16 and 110

L11 16 L6 AND L10

=> s 12 and 110

85 L2 AND L10

=> s 12 and 17

1.13 15 L2 AND L7

=> s 111 or 112 or 113

94 L11 OR L12 OR L13

=> dup rem 114

PROCESSING COMPLETED FOR L14

74 DUP REM L14 (20 DUPLICATES REMOVED)

=> s 115 and py<2000

1 FILES SEARCHED...

3 FILES SEARCHED...

4 FILES SEARCHED

60 L15 AND PY<2000 L16

=> dup rem 111

PROCESSING COMPLETED FOR LIT

10 DUP REM L11 (6 DUPLICATES REMOVED)

=> d 18 ibib abs 1-10

L8 ANSWER I OF 5 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-089629 [12] WPIDS

C2002-027553 DOC. NO. CPI:

TITLE:

Cryopreservation of cells involves contacting cells with ***cyclohexanediol*** compound, and

subsequently reducing the temperature of cells to ***cryopreservation*** temperature.

DERWENT CLASS: B04 D22 E15

INVENTOR(S): BROCKBANK, K G M; CAMPBELL, L H;

TAYLOR, M J

PATENT ASSIGNEE(S): (ORGA-N) ORGAN RECOVERY SYSTEMS

INC; (BROC-I) BROCKBANK K

G M; (CAMP-I) CAMPBELL L H; (TAYL-I) TAYLOR M J

COUNTRY COUNT: 95 PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2001078505 A1 20011025 (200212)* EN 20

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ

LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD

SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW AU 2001055433 A 20011030 (200219)

US 2002068360 A1 20020606 (200241)

APPLICATION DETAILS:

PATENT NO KIND APPLICATION DATE

WO 2001078505 A1 WO 2001-US12465 20010417 AU 2001055433 A AU 2001-55433 20010417 US 2002068360 A1 Provisional US 2000-197669P 20000417

US 2001-835818 20010417

FILING DETAILS:

PATENT NO KIND

PATENT NO

AU 2001055433 A Based on WO 200178505

PRIORITY APPLN. INFO: US 2000-197669P 20000417; US 2001-835818

20010417 AN 2002-089629 [12] WPIDS

AB WO 200178505 A UPAB: 20020221

NOVELTY - Cells are ***cryopreserved*** by contacting the cells

cryopreservation composition containing

cyclohexanediol

(CHD) compound, and subsequently reducing the temperature of the cells

a ***cryopreservation*** temperature.

USE - For ***cryopreservation*** of cells.

ADVANTAGE - The method increases cell viability upon warming

from a frozen state.

Dwg.0/5

L8 ANSWER 2 OF 5 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-317282 [27] WPIDS CROSS REFERENCE: 2000-303114 [24]

C2000-095882 DOC, NO, CP1:

New ***cryopreservative*** solutions, useful for ***preserving*** biological samples such as cells, TITLE:

embryos, tissues, organs and animals.

DERWENT CLASS: A96 B04 D16 D22

FAHY, G M; WOWK, B INVENTOR(S):

PATENT ASSIGNEE(S): (TWOO-N) 21ST CENTURY MEDICINE INC;

(FAHY-I) FAHY G M;

(WOWK-I) WOWK B COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000016618 A1 20000330 (200027)* EN 46 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE

LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS

LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ

TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000010939 A 20000410 (200035)

EP 1115281 A1 20010718 (200142) EN R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV

MC MK NL RO

US 6395467 B1 20020528 (200243)

APPLICATION DETAILS:

PATENT NO KIND

APPLICATION DATE

WO 2000016618 A1 AU 2000010939 A EP 1115281 A1

WO 1999-US21736 19990921 AU 2000-10939 19990921 EP 1999-954636 19990921

WO 1999-US21736 19990921

US 6395467 B1 Provisional US 1998-101194P 19980921

US 1999-127158P 19990331 Provisional US 1999-128142P 19990407 Provisional US 1999-143587P 19990713 Provisional US 1999-400793 19990921

FILING DETAILS:

PATENT NO KIND

PATENT NO

AU 2000010939 A Based on WO 200016618 EP 1115281 A1 Based on WO 200016618

PRIORITY APPLN, INFO: US 1999-143587P 19990713; US 1998-101194P

19980921: US 1999-127158P 19990331: US 1999-128142P 19990407; US 1999-400793 19990921

AN 2000-317282 [27] WPIDS

CR 2000-303114 [24]

AB WO 200016618 A UPAB: 20020709

NOVELTY - New ***cryopreservation*** solutions are obtained by changing the components of solutions and determining the effect on toxicity, vitrification and ability to resist devitrification.

DETAILED DESCRIPTION - A novel solution for

cryopreservation

of biological samples comprises at least one ***cryoprotective*** agent for which qv is between 1 and 2, where the total concentration of the ***cryoprotective*** agent is between 5 and 150 % of its Cv; and where the toxicity of the solution for ***cryopreservation*** causes at most 50% reduction in viability as measured in a kidney slice assay.

qv = the moles of water per mole of polar group at Cv;

Cv = the concentration needed to vitrify 5-10 ml of the solution at a cooling rate of 10 deg. C/minute.

INDEPENDENT CLAIMS are also included for:

(1) a method for producing optimal solutions for vitrification comprising: (a) selecting dimethylsulfoxide and formamide in a molar ratio of 1.1-0.8 and at a total concentration of 30-45% w/v; (b) selecting an additional penetrating ***cryoprotective*** whose qv is below 2; (c) adding the additional penetrating ***cryoprotective*** agent to the dimethylsulfoxide and formamide in varying concentrations; (d) cooling the

resulting mixtures so as to determine the concentration of the additional ***cryoprotective*** agent to vitrify the solution; (e) subtracting 2-6% w/v of the additional ***cryoprotective*** agent; (f) replacing the 2-6% w/v of subtracted additional ***cryoprotective*** agent with

w/v non-penetrating agent; and (g) adding a fourth penetrating ***cryoprotective*** agent if the solution does not vitrify to restore the solution to its Cv; (h) exposing the biological system to the discovered vitrification solution with or without subsequent vitrification; and (i) testing the biological sample for viability;

- (2) a method for optimizing the ***freezing*** of biological systems comprising: (a) selecting an optimum vitrification solution as in (1); (b) exposing the biological system to a dilution of the vitrification solution yielding a final concentration of penetrating agent of 2-35% w/v, or of 0.2-4M; and (c) cooling the system;
- (3) a ***cryoprotectant*** solution comprising dimethyl sulfoxide, an amide or a combination of amides, and at least one penetrating ***cryoprotective*** chemical where the qv of the solution in aqueous solution is below 1.9 and where the toxicity of the solution at its ov is less than the toxicity of VS41A:
- (4) a ***cryoprotective*** solution comprising dimethyl sulfoxide and at least 2 penetrating ***cryoprotective*** chemicals where the qv values of the penetrating ***cryoprotective*** chemicals in aqueous solution are below 1.9 for each ***cryoprotective*** chemical, or where the vitrification to a cooling rate of approx. 30 deg. C/minute or less, and where the ***cryoprotective*** solution is less toxic than VS41A:
- (5) a vitrification solution comprising dimethyl sulfoxide, an amide or combination of amides, and at most 16% w/v 1,2-propanediol;
- (6) a ***cryoprotectant*** solution having a qv of at most 1.9;
- (7) a method of ***preserving*** a living system by supercooling, comprising: (a) distributing through the system a non-toxic amount of

polyvinyl alcohol, at a concentration of 0.01-6% w/v, in combination with a concentration of ***cryoprotectant*** to allow supercooling of the living system at the desired storage temperature, which concentration of ***cryoprotectant*** may range from 0-60% w/v, at a temperature

from -20 to 37 deg. C; (b) cooling the living system to the storage temperature, ranging from 0 to -100 deg. C; (c) storing the system; (d) warming the system back to -20 to 37 deg. C; and (e) removing the

- ***cryoprotectant*** and polyvinyl alcohol;

 (8) a ***cryoprotectant*** solution comprising a concentration of urea to eliminate devitrification at a warming rate of 70 deg. C/minute or less when the solution is at its Cv;
- (9) a method for composing vitrification solutions containing non-penetrating high molecular weight polymers (over 11000 daltons in mass), comprising: (a) subtracting 1-7% of the penetrating
 cryoprotectant that would otherwise be needed to vitrify; and (b)
- replacing this penetrating ***cryoprotectant*** with 2-8% w/v of the high molecular weight polymer;
- (10) a method for selecting good candidate ***cryoprotectant*** solutions from poor candidate solutions comprising: (a) determining the total concentrations of the candidate solutions that are needed to vitrify; (b) determining the qv of the solutions; (c) ranking the solutions based on their qv values; and (d) preferentially testing solutions having the lower qv values.

USE - The solutions can be used for ***preserving*** biological samples, e.g. cells, embryos, tissues, organs or animals (claimed), They can also be used for the ***cryopreservation*** of proteins, organelles, cell extracts, blood vessels, artificial or engineered cells, tissues, blood vessels, organs or organoids, or other biological systems by vitrification, ***freezing*** or other means.

ADVANTAGE - The solutions can provide for ***cryoprotection*** while minimizing toxicity without weakening their ability to vitrify and to resist devitrification.

Dwg.0/10

L8 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:780597 HCAPLUS

DOCUMENT NUMBER: 135:328945

TITLE: Cyclohexanediols as ***cryoprotectant*** compounds INVENTOR(S): Brockbank, Kelvin G. M.; Taylor, Michael J.; Campbell,

PATENT ASSIGNEE(S): Organ Recovery Systems, Inc., USA

Lia Hanson SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001078505 A1 20011025 WO 2001-US12465 20010417 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002068360 A1 20020606 US 2001-835818 20010417 US 2000-197669P P 20000417 PRIORITY APPLN. INFO.:

AB A method of ***cryopreserving*** cells includes bringing the cells into contact with a ***cryopreservation*** compn. contg. at least one ***cyclohexanediol*** compd., and subsequently reducing the temp. of

cells to a ***cryopreservation*** temp. The at least one ***cyclohexanediol*** compd. is preferably the cis or trans forms of ***|*** , ***3*** - ***cyclohexanedio|*** or ***|*** , ***4*** - ***cyclohexanediol***, and racemic mixts, thereof. A preferred ***cryopreservation*** compn. includes the at least one

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***cyclohexanediol*** compd. and at least one addnl.
    ***cryoprotectant*** compd. The viability of porcine heart valve
   leafters stored at -135.degree. in presence of ***|***. ***3*** -
***cyclohexanediol*** or ***|***, ***4*** -
***cyclohexanediol***
   was shown.
REFERENCE COUNT:
                         4 THERE ARE 4 CITED REFERENCES
AVAILABLE FOR THIS
                RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT
L8 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                          2000:209818 HCAPLUS
DOCUMENT NUMBER:
                           132:255981
                 Improved ***cryoprotectant*** solutions
TITLE:
INVENTOR(S):
                     Wowk, Brian; Fahy, Gregory M.
PATENT ASSIGNEE(S): 21st Century Medicine, Inc., USA
SOURCE:
                   PCT Int. Appl., 47 pp.
             CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                     English
FAMILY ACC, NUM. COUNT: 1
PATENT INFORMATION:
   PATENT NO. KIND DATE
                                     APPLICATION NO. DATE
   WO 2000016618 A1 20000330
                                     WO 1999-US21736 19990921
     W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
CN. CR.
       CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD,
GE,
       GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK,
       LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO,
       RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
UZ.
       VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
     RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
CY, DE,
       DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
       CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                    WO 1999-US21967 19990921
   WO 2000016619 AT 20000330
     W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH,
       CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD,
GE,
       GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK,
       LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO,
       RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
UZ,
       VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
     RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
CY. DE.
       DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
       CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
   AU 9964992
                 A1 20000410 AU 1999-64992 19990921
   EP 1115281
                 A1 20010718
                                  EP 1999-954636 19990921
     R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE,
       LT, LV, FI, RO
   US 6391224
                 B1 20020521
                                  US 1999-400791 19990921
   US 6395467
                 B1 20020528
                                  US 1999-400793 19990921
PRIORITY APPLN. INFO.:
                                  US 1998-101194P P 19980921
                     US 1999-127158P P 19990331
                     US 1999-128142P P 19990407
                     US 1999-143587P P 19990713
                     WO 1999-US21736 W 19990921
                     WO 1999-US21967 W 19990921
AB Surprising new combinations of previously-known and novel
    ***cryoprotectants*** are provided that yield superior recovery of
   function and viability of living systems after exposure to and removal
   from said systems. These and related combinations are useful for
    ****cryopreservation*** by vitrification, ***freezing***,
  supercooling, f.p. depression, or cold storage. Contrary to current opinion, ideal solns. for ***cryopreservation*** are those that
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vitrify "poorly" (i.e., at higher rather than at lower concns.). By using
   relatively "poor" vitrifiers, the water content of the soln. is reduced at
   the concn. needed to vitrify, but the water availability within the soln.
   is believed to be paradoxically increased, thereby increasing viability.
   A novel method for understanding and predicting non-specific
     ***cryoprotectant*** toxicity is provided based on a new definition of
    ***cryoprotectant*** "concn.", which is the no. of water mols./polar
   group on penetrating ***cryoprotectants*** . Compns. are provided
   vitrify at relatively high concns., yet surprisingly also devitrify slowly
   on warming. Databases of novel vitrification/devitrification and toxicity
   data are provided that allow the ordinary practitioner of the art to
   select specific solns, or obvious soln, variants to meet the user's
   specific ***cryopreservation*** needs. The addn. of ethylene glycol
   to the ***cryoprotectant*** solns. damaged or killed only 10% corneal
   endothelial cells, whereas without ethylene glycol 20% of the cells were
   killed.
REFERENCE COUNT:
                            5 THERE ARE 5 CITED REFERENCES
AVAILABLE FOR THIS
                  RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT
L8 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
                             1967:443383 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                              67:43383
TITLE:
                  Synthesis of esters of .alpha.,.alpha.-dimethyl
              alkanoic acids
AUTHOR(S):
                      Zharova, E. Ya.; Puzitskii, K. V.; Rapoport, I. B.;
               Eidus, Ya. T.; Velizar'eva, N. I.
SOURCE:
                    Neftekhimiya (1967), 7(1), 92-6
               CODEN: NEFTAH
DOCUMENT TYPE:
                           Journal
LANGUAGE:
                        Russian
AB Neo acids (.alpha...alpha.-dimethyl acids) were prepd. by carboxylation
   olefins or monovalent satd, alcs, with CO at 40.degree./30-50 atm, in the
   presence of H2SO4. Homologs C13 (b17 165-200.degree.) and C16 (b10
   165-98.degree.) were prepd. from tetramers or pentamers of propylene.
   acids were then converted to the corresponding acid chlorides in 80-90%
   yield by adding excess SO2Cl2 dropwise at 76-9.degree.. The prepd. neo
   acids have the following b.p./mm., d20, and n20D: C5, 47-9.degree./10,
   0.9676, 1.4312; C8, 57-8.degree./10, 0.9571, 1.4349; C9,
74-6.degree./10.
   0.9497, -; C10, 90-1.5.degree./10, 0.9435, 1.4422; C11, 125-6.degree./21,
   0.9347, 1.4443. Alcs. were acylated with acid chlorides at
   50-100.degree., HCl was removed at 100.degree. with N, the products
   washed with NaOH and Na2CO3 solns., then with water, and
fractionated.
   The yields were 85-95% with respect to acid chloride and 70-90% with
   respect to neo acid. Crude ***1*** , ***3*** -
    ***cyclohexanediol*** esters contain monoesters and 65% diesters.
   Monoesters, ***freezing*** between -63 and -49.degree., have the
   following b.p. at 1-2 mm., n20D, and viscosity at 50.degree. in
   centistokes: C7, 105-68.degree., 1.4539, 8.2; C8, 120-80.degree., 1.4572,
   6.4; C9, 135-92.degree., 1.4612, -; C10, 137-98.degree., 1.4608, 10.2;
   C11, 106-209.degree., 1.4612, 10.0. Analogously, the same values of
   diesters ***freezing*** between -46 and -40.degree. are as follows:
   C7, 168-70.degree., 1.4535, 9.5; C8, 180-1.degree., 1.4549, 11.2; C9,
   192-4.degree., 1.4579, 15.9; C10, 198-200.degree., 1.4587, 21.8; C11,
   209-11.degree., 1.4600, 24.4. These characteristics are further given for
   the esters of neo acids and polyols: C8, (CH2)6(OH)2 178-80.degree.,
   1.4430, 7.0; C7, (CH2)10(OH)2 192-4.degree., 1.4452, 8.6; C8,
(CH2)10(OH)2
   202-5.degree., 1.4481, 10.0; C7, trimethylolpropane, 213-24.degree.,
   1.4490-1.4509, 18.9-22.9. Diol esters ***freeze*** at the temp.
   between -63 and -69.degree., the triol ester at -45.degree.. The esters
   of 2-ethyl-1-hexanol and neo acids ( *** freezing *** at -67.degree. or
   lower) have the following characteristics (ordered in the above sequence):
   C7, 112-14.degree., 1.4330, 2.0; C9, 114-16.degree., 1.4365, 2.4; C13,
   154-60.degree., 1.4460, 5.7; C16, 156-66.degree., 1.4510, 7.0. Mixts. of
   esters of C7 neo acid and 2-ethyl-1-hexanol and ***1*** , ***3***
    ***cyclohexanedioi*** have improved phys. properties. Thus, the
mixt.
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of these esters in the ratio ***1*** : ***4*** ***freezes*** at

-63.degree. and has visocisity 6.06 centistokes at 50.degree..

(FILE 'HOME' ENTERED AT 12:33:13 ON 29 AUG 2002) FILE 'BIOSIS, EMBASE, MEDLINE, WPIDS, HCAPLUS' ENTERED AT 12:33:22 ON 29 AUG 2002 **0 S 13CYCLOHEXANEDIOL AND 14CYCLOHEXANEDIOL** LI L2 2514 S CYCLOHEXANEDIOL L3 1847673 S "1,3" 1415573 S "1,4" L4 162390 S L3 AND L4 1.5 1.6 444 S L2 AND L5 L.7 846158 S FREEZ? OR PRESERV? OR CRYO? L8 5 S L6 AND L7 3 DUP REM L8 (2 DUPLICATES REMOVED) L10 11943103 S CELL OR CELLS OR CELLULAR OR TISSUE? LII 16 S L6 AND L10 L12 85 S L2 AND L10 L13 15 S L2 AND L7 L14 94 S L11 OR L12 OR L13 74 DUP REM L14 (20 DUPLICATES REMOVED) LI5 L16 60 S L15 AND PY<2000

10 DUP REM L11 (6 DUPLICATES REMOVED) L17

=> s 115 not 117 L18 64 L15 NOT L17

=> dup rem 118

PROCESSING COMPLETED FOR L18

64 DUP REM L18 (0 DUPLICATES REMOVED) 1.19

=> s 116 not 117 L20 54 L16 NOT L17

=> d 120 ibib abs 1-54

L20 ANSWER I OF 54 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:301644 BIOSIS DOCUMENT NUMBER: PREV200000301644

Process for making metabolites of lycopene. AUTHOR(S): Pfander, Hanspeter (1); Traber, Bruno CORPORATE SOURCE: (1) Bern Switzerland

ASSIGNEE: Roche Vitamins Inc. PATENT INFORMATION: US 6008417 December 28, 1999

SOURCE: Trademark

Official Gazette of the United States Patent and

Office Patents, (***Dec. 28, 1999***) Vol. 1229, No. 4, pp. No pagination. e-file. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

AB The invention is concerned with a multi-stage process for making an oxidative metabolite of the carotenoid lycopene, 2,6-cyclolycopene-1,5diol having the formula ##STR1## In this process alpha-terpinyl acetate is oxidatively dihydroxylated to a ***cyclohexanediol*** (IV), the ***cyclohexanediol*** (IV) is oxidatively cleaved to a ketoaldehyde

the ketoaldehyde (V) is subjected to an intramolecular aldol condensation to give a cyclopentanol (VI), the cyclopentanol (VI) is silylated to its silylated derivative formylcylopentane (VII), the formylcyclopentane (VII) is subjected to a C3 -chain lengthening with acetone and simultaneously to a saponification for the cleavage of the acetyl group to give a cyclopentylbutenone (VIII), the cyclopentylbutenone (VIII) is reacted with vinyl magnesium bromide to give a pentadienol (IX), the pentadienol (IX) is converted with deprotection of the silylated hydroxy group into a phosphonium salt (X), this salt is subjected to a Wittig reaction with 2,7-dimethyl-2,4,6-octatriene-1,8-dial to give a tridecahexaenal (XII) and the tridecahexaenal (XII) is subjected to a Wittig reaction with a (3,7,11-trimethyl-dodeca-2,4,6,10-tetraenyl)triphenylphosphonium salt to give the desired 2,6-cyclolycopene-1,5-diol (II). A variant of this process, also in accordance with the invention, comprises converting the cyclopentylbutenone (VIII) into the phosphonium salt (X) via two alternative intermediates, namely a pentadienoic acid ester (XIV) and a different pentadienol (XV), into the same phosphonium salt (X).

the invention is concerned with the novel intermediates (V), (VI), (VII),

(VIII), (IX), (X), (XII), (XIV) as well as (XV) and the individual process steps which lead to these novel intermediates. 2,6-cyclolycopene-1,5-diol is useful in the prevention of cancer growth in human ***cells*** .

L20 ANSWER 2 OF 54 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC

ACCESSION NUMBER: 1994:234524 BIOSIS DOCUMENT NUMBER: PREV199497247524

Simple and sensitive determination of 2,3-butanediol in biological samples by gas chromatography with electron-capture detection.

AUTHOR(S): Otsuka, Masato; Ohmori, Shinjii (1)

CORPORATE SOURCE: (1) Faculty Pharmaceutical Sciences, Okayama University,

Tsushima-Naka-I-I, Okayama 700 Japan

SOURCE: Journal of Chromatography B Biomedical Applications, (1994)

Vol. 654, No. 1, pp. 1-7.

DOCUMENT TYPE: Article LANGUAGE: English

AB 2,3-Butanediol was quantitatively oxidized into diacetyl by reaction with MnO-4- at 20 degree C for 30 min under neutral conditions. The reaction

diacetyl with 4,5-dichloro-1,2-diaminobenzene afforded 6,7-dichloro-2,3-dimethyl-quinoxaline (DCDMQ), which was extracted with

n-hexane and determined by gas chromatography with electron-capture detection. As an internal standard 1,2- ***cyclohexanediol*** was used. The detection limit of DCDMQ (or 2,3-butanediol) was 10 fmol/mu-l in

extract, and the determination limit of DCDMQ (or 2,3-butanediol) was at least from 50 fmol/mu-l to 20 pmol/mu-l in the extract. Recoveries from normal rat urine and rat liver homogenate were 97.8 +- 3.4% and 98.4 +-2.9%, respectively. The method is very simple and sensitive and is applicable to the determination of 2,3-butanediol in normal rat **tissues***

L20 ANSWER 3 OF 54 BIOSIS COPYRIGHT 2002 BIOLOGICAL

ABSTRACTS INC.

ACCESSION NUMBER: 1989:243885 BIOSIS DOCUMENT NUMBER: BA87:124950

OXIDATION OF TRANS AND CIS-1 2 TITLE: ***CYCLOHEXANEDIOL*** BY

GLUCONOBACTER-OXYDANS PREPARATION OF R

AND S-2

HYDROXYCYCLOHEXANONE.

AUTHOR(S): ADLERCREUTZ P

CORPORATE SOURCE: DEP. OF BIOTECHNOL., CHEM. CENT., UNIV. OF LUND, P.O. BOX

124, S-22100 LUND, SWEDEN.

SOURCE: APPL MICROBIOL BIOTECHNOL, (1989) 30 (3), 257-263.

CODEN: AMBIDG. ISSN: 0175-7598.

FILE SEGMENT: BA; OLD LANGUAGE: English

AB The enzymatic oxidation of 1,2- ***cyclohexanediol*** and related substrates by Gluconobacter oxydans (ATCC 621) was investigated. At

pH, membrane-bound enzymes were active and at high pH, NAD-dependent,

soluble enzymes showed activity. Whole bacterial ***cells*** were used

to catalyze some bioconversions. Racemic trans-1,2-

cyclohexanediol

was oxidized at pH 3.5 to give (R)-2-hydroxycyclohexanone (96% e.e.)

at pH 8.0 the same substrate was oxidized to (S)-2-hydroxycyclohexanone (97% e.e.). The latter conversions was severely inhibited by the reaction product while the former was not significantly product inhibited. (S)-2-hydroxycyclohexanone (97% e.e.) was also prepared from cis-1,2-***cyclohexanediol*** by oxidation with G. oxydans ***cells*** at

3.5 in a reaction which continued to 100% conversion.

L20 ANSWER 4 OF 54 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1982:306077 BIOSIS DOCUMENT NUMBER: BA74:78557

TITLE: MYO INOSITOL TRANSPORT IN

SACCHAROMYCES-CEREVISIAE.

AUTHOR(S): NIKAWA J-I; NAGUMO T; YAMASHITA S CORPORATE SOURCE: DEP. BIOCHEM., GUNMA UNIV. SCH. MED., MAEBASHI 371, JAPAN.

J BACTERIOL, (1982) 150 (2), 441-446. SOURCE:

CODEN: JOBAAY. ISSN: 0021-9193.

FILE SEGMENT: BA; OLD LANGUAGE: English

AB myo-Inositol uptake in S. cerevisiae was dependent on temperature, time and substrate concentration. The transport obeyed saturation kinetics with an apparent Km for myo-inositol of 0.1 mM. myo-Inositol analogs, such as scyllo-inositol, 2-inosose, mannitol, and 1,2- ***cyclohexanediol*** had no effect on myo-inositol uptake. myo-Inositol uptake required metabolic energy. Removal of D-glucose resulted in a loss of activity, and azide and cyanide ions were inhibitory. In the presence of D-glucose, myo-inositol was accumulated in the ***cells*** against a concentration gradient. A myo-inositol transport mutant was isolated against a concentration gradient. A myo-inositol transport mutant was isolated from UV-mutagenized S. cerevisiae ***cells*** using the replica-printing technique. The defect in myo-inositol uptake was due to a single nuclear gene mutation. The activities of L-serine and D-glucose transport were not affected by the mutation. Thus it was shown that S. cerevisiae grown under the present culture conditions possessed a single and specific myo-inositol transport system, myo-Inositol transport activity was reduced by the addition of myo-inositol to the culture medium. The activity was reversibly restored by the removal of myo-inositol from the medium. This restoration of activity was completely abolished by cycloheximide.

L20 ANSWER 5 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1998097919 EMBASE

TITLE: Glucose transport inhibitors protect against

1,2-cyclohexanedione-produced potassium loss from human red blood ***cells***

AUTHOR: Baker G.F.; O'Gorman R.; Baker P.

CORPORATE SOURCE: G.F. Baker, Department of Biological Sciences, Royal

Holloway, University of London, Egkam TW20 0EX, United

Kingdom. g.baker@rhbnc.ac.uk

SOURCE: Experimental Physiology, (1998) 83/2 (239-242).

Refs: 5

ISSN: 0958-0670 CODEN: EXPHEZ

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

002 Physiology FILE SEGMENT: Clinical Biochemistry 029

LANGUAGE: English SUMMARY LANGUAGE: English

AB It has been suggested that the glucose transport system of human erythrocytes contains an arginine shield to prevent the leak of potassium through the transporter. To investigate this suggestion we treated human erythrocytes with the specific arginine reagent 1,2-cyclohexanedione. Under conditions which produce a covalent reaction between arginine and the reagent, a steady leak of potassium occurs. If glucose, maltose or the inhibitor phloretin are present during the reaction the extent of the leak is reduced. These findings support the view that arginines have a role in preventing potassium loss through the glucose transporter.

L20 ANSWER 6 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

ACCESSION NUMBER: 1998043017 EMBASE

Effect of the chemical modification of the arginyl residue TITLE: in Bombyx mori silk fibroin on the attachment and growth of fibroblast ***cells***

AUTHOR: Gotoh Y.; Tsukada M.; Minoura N.

CORPORATE SOURCE: Y. Gotoh, National Institute of Sericultural, Entomological

Science, 1-2 Ohwashi, Tsukuba, Ibaraki 305, Japan

SOURCE: Journal of Biomedical Materials Research, (1998) 39/3 (351-357)

Refs: 18

ISSN: 0021-9304 CODEN: JBMRBG

COUNTRY: United States DOCUMENT TYPE: Journal; Article

027 Biophysics, Bioengineering and Medical FILE SEGMENT:

Instrumentation

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LANGUAGE:
               English
SUMMARY LANGUAGE: English
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AB We prepared matrices of Bombyx mori silk fibroin (SF) with different degrees of modification of arginyl residues by reaction between 1,2cyclohexanedione (CHD) and SF. Two kinds of SF, namely native SF (NSF).

obtained from the silk gland of silkworm larvae, and regenerated SF (RSF),

prepared from cocoons of the same silkworm, were used in this study because their amino acid compositions were slightly different from each other. The attachment and growth of mouse fibroblast (L-929)

cells on the matrices of the NSF and RSF, in which half or almost all of the arginyl residues were modified (NSF50, RSF50, NSF100, and RSF100),

studied using a ***cell*** culture method. Both NSF50 and NSF100 exhibited higher ***cell*** attachment than did the unmodified NSF. While the ***cell*** growth on NSF50 was not significantly different from that on NSF and NSF100, the growth on NSF100 was higher than that on

NSF. The ***cells*** attached to NSF50 and NSF100 were extensively spread out and their filopodia were visible by SEM. The ***cell** attachment and growth on RSF were comparable to those on NSF100.

RSF50 exhibited almost the same ***cell*** attachment as did the unmodified RSF, RSF100 exhibited a lower ***cell*** attachment than did the unmodified RSF and RSF50. There were no significant differences

the ***cell*** growth among RSF series. The ***cells*** attached to RSF50 and RSF100 aggregated to form masses, and their filopodia could

not be found. The relationship of ***cell*** attachment to the basicity of the substrate is considered because the modification of the positively charged arginyl residue changed the basicity of the substrate and the ***cell*** attachment on the substrate.

L20 ANSWER 7 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V. ACCESSION NUMBER: 97268434 EMBASE

DOCUMENT NUMBER: 1997268434 TITLE: Modification of arginine-198 in sarcoplasmic reticulum

Ca2+-ATPase by 1,2-cyclohexanedione causes inhibition of formation of the phosphoenzyme intermediate from inorganic phosphate.

AUTHOR: Saino T.; Daiho T.; Kanazawa T.

CORPORATE SOURCE: T. Kanazawa, Department of Biochemistry, Asahikawa Medical

College, Nishikagura Asahikawa 078, Japan.

kanazawa@asahikawa-med.ac.jp

SOURCE: Journal of Biological Chemistry, (1997) 272/34

(21142-21150). Refs: 46

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Sarcoplasmic reticulum vesicles were modified with I,2-cyclohexanedione

and

(CHD), a specific arginine-modifying reagent, in sodium borate (pH 8.0 or 8.8). Phosphoenzyme formation from P(i) in the Ca2+-ATPase (reversal of hydrolysis of the phosphoenzyme intermediate) was almost completely inhibited by the modification with CHD. Tight binding of F- and Mg2+

high affinity binding of vanadate in the presence of Mg2+, either of which produces a transition state analog for phosphoenzyme formation from the magnesium-enzyme-phosphate complex, were also markedly inhibited. In contrast, phosphoenzyme formation from acetyl phosphate in the forward reaction was unaffected. The enzyme was appreciably protected by tight binding of F- and Mg2+ or by high affinity binding of vanadate in the presence of Mg2+, but not by the presence of 20 mM MgC12 alone or 150

P(i) alone, against the CHD-induced inhibition of phosphoenzyme

from P(i). Peptide mapping of the tryptic digests, detection of peptides containing CHD-modified arginyl residues with Girard's reagent T, sequencing, and mass spectrometry showed that Arg-198 was a single

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major
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residue protected by tight binding of F- and Mg2+ against the modification with CHD. These results indicate that modification of Arg-198 with CHD

is

responsible for at least a part (the portion reduced by the transition state analogs) of the CHD-induced inhibition of phosphoenzyme formation from P(i) and suggest that Arg-198 is located in or close to the catalytic site in the transition state for phosphoenzyme formation from the magnesium-enzyme- phosphate complex.

L20 ANSWER 8 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96348066 EMBASE

DOCUMENT NUMBER: 1996348066

TITLE: Identification of arginyl residues located at the ATP binding site of sarcoplasmic reticulum Ca2+-ATPase:

Modification with 1,2-cyclohexanedione.

AUTHOR: Kimura K.; Suzuki H.; Daiho T.; Yamasaki K.; Kanazawa

CORPORATE SOURCE: Dept. of Biochemistry, Asahikawa Medical College, Nishikagura, Asahikawa 078, Japan

SOURCE: Journal of Biological Chemistry, (1996) 271/46

(28933-28941).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Sarcoplasmic reticulum vesicles were treated with 1,2-cyclohexanedione (CHD) in sodium borate (pH 8.0). The Ca2+-ATPase activity was completely

inhibited. Inhibition of Mg.cntdot.ATP and Mg.cntdot.ADP binding to the high affinity ATP binding site as well as inhibition of phosphorylation with ATP occurred simultaneously with the inhibition of the Ca2+-ATPase activity. Phosphorylation with acetyl phosphate was not inhibited. The Ca2+-ATPase was strongly protected by Mg.cntdot.ATP,

Mg.cntdot.ADP, and

Mg.cntdot.AMP against this inhibition. Binding of acetyl phosphate or P(i) to the enzyme gave no protection. Phosphorylation with acetyl phosphate also had no protective effect. Peptide mapping of the tryptic digests, detection of peptides containing CHD-modified arginyl residues with Girard's reagent T, and sequencing revealed that Arg-489, Arg-505, and Arg-678 were modified with CHD. Arg-489 and Arg-678 were almost completely

protected by Mg. ATP against this modification, but partially protected by prelabeling with fluorescein 5- isothiocyanate, which occupies the adenosine binding region in the ATP binding site. In contrast, Arg-505

slightly protected by Mg-ATP and almost completely protected by prelabeling with fluorescein 5-isothiocyanate. Taken together, these findings suggest that Arg-489 and Arg-678 are located in or near the region occupied by the triphosphate moiety of ATP, either or both of these residues being in or close to the region occupied by the .alpha.-phosphoryl group in the high affinity ATP binding site and involved in the CHD-induced inhibition of this enzyme and that Arg-505 is very close to (but slightly out of) the adenosine binding region in the ATP binding site. The acetyl phosphatase activity and phosphorylation with P(i) were also inhibited by the CHD treatment, but the inhibitions were considerably slower than those described above. This suggests that the arginyl residues involved in these inhibitions are distinct from that involved in the inhibition of the Ca2+- ATPase activity.

L20 ANSWER 9 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 96263203 EMBASE DOCUMENT NUMBER: 1996263203

TITLE: Metabolic fate of TCV-116, a new angiotensin II receptor antagonist, in rats and dogs.

AUTHOR: Kondo T.; Hagihara K.; Kato Y.; Yoshida K.; Yoshimura

Motohashi M.; Tanayama S.

SOURCE: Japanese Pharmacology and Therapeutics, (1996)

24/SUPPL. 6

(139-165).

ISSN: 0386-3603 CODEN: YACHDS

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Pharmacology 037 Drug Literature Index

LANGUAGE: Japanese

SUMMARY LANGUAGE: English; Japanese

AB After oral administration of 14C labeled TCV-116 ([14C]TCV-116) to rats

and dogs, TCV-116 was absorbed from the small intestine and hydrolyzed completely to the pharmacologically active metabolite. M-I (CV-11974), during absorption process. The bioavailabilities of the drug as M-I were 19-28 and 5% in rats and dogs (both fed), respectively. In dogs, bioavailability increased to 18% by starvation. The concentration of M-I in plasma of rats attained a peak (C(max) 0.280 .mu.g/ml) 2.3 hr (T(max)) after dosing, and then declined with an apparent half life (t(1/2)) of 3.8 hr. In dogs, T(max), C(max), and t(1/2) of M-I were 1.3 hr, 0.012 .mu.g/ml, and 4.3 hr, respectively. The pharmacokinetics of M-I in rats and dogs were linear in a dose range of 1 to 100 mg/kg. In rats given [14C]TCV-116 orally, 14C was widely distributed in the bodies, with relative high concentration of plasma, gastrointestinal tract, liver, kidney, lung, and pituitary gland. The major component in rat

target ***tissue*** . M-I and other metabolites were transferred into rat fetus and milk. M-I and its metabolites extensively bound to plasma proteins of rats and dugs, and serum proteins of humans. No protein binding interaction between TCV-116 metabolites (M-I and M-II and propranolol, nifedipine, manidipine hydrochloride, trichlormethiazide, hydrochlorothiazide, digoxin, furosemide, and mexiletine was observed in human serum albumin. M-I was partly metabolized to M-II and M-I glucuronides (M-I NG and M-I AG). After oral administration of TCV-116

M-I and other metabolites were excreted predominantly in fetes via hepatobiliary route in rats and dogs. On repeated dosing of I4CITCV-116.

no appreciable amount of 14C related materials was accumulated in the bodies of rats. Daily oral administration of TCV-116 to rats resulted in no effect on the drug metabolizing enzymes. The ester side chain of TCV-116 was absorbed mainly as cyclohexanol and distributed widely in ***tissues*** . Cyclohexanol was excreted largely in urine after metabolized partly to ***cyclohexanediol***, cyclohexanetriol, and other metabolites.

L20 ANSWER 10 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 94303674 EMBASE

DOCUMENT NUMBER: 1994303674

TITLE: Purification and characterization of dimeric dihydrodiol

dehydrogenase from dog liver.

AUTHOR: Sato K.; Nakanishi M.; Deyashiki Y.; Hara A.; Matsuura K.;

k.; Ohya I.

CORPORATE SOURCE: Biochemistry Laboratory, Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502, Japan

SOURCE: Journal of Biochemistry, (1994) 116/3 (711-717).

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB High NADP+-linked dihydrodiol dehydrogenase activity was detected in dog

liver cytosol, from which a dimeric enzyme composed of M(r) 39,000 subunits was purified to homogeneity. The enzyme oxidized trans***cyclohexanediol***, and trans-dihydrodiols of benzene and naphthalene, the [1R,2R]-isomers of which were selectively oxidized. In the reverse reaction in the presence of NADPH as a coenzyme, the

reduced .alpha.-dicarbonyl compounds, such as methylglyoxal, 3-deoxyglucosone, and diacetyl, and some compounds with a carbonyl group,

such as glyceraldehyde, lactaldehyde, and acetoin.

4-Hydroxyphenylketones

and ascorbates inhibited the enzyme. The results of steady-state kinetic analyses indicated that the reaction proceeds through an ordered bi bi mechanism with the coenzyme binding to the free enzyme, and suggested at

the inhibitors bind to the enzyme-NADP+ binary complex. The dimeric enzyme

was detected in liver and kidney of dog, and was immunochemically similar

to the dimeric enzymes from monkey kidney, rabbit lens, and pig liver. The

sequences (total 127 amino acid residues) of eight peptides derived on enzymatic digestion of the dog liver enzyme did not show significant similarity with the primary structures of members of the aldo-keto reductase and short chain dehydrogenase superfamilies, which include monomeric dihydrodiol dehydrogenases and carbonyl reductase, respectively.

L20 ANSWER II OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 93237216 EMBASE DOCUMENT NUMBER: 1993237216

TITLE: The inhibition of glucose exits in human erythrocytes by

1,2-cyclohexanedione.

AUTHOR: Baker G.F.; Widdas W.F.

CORPORATE SOURCE: Department of Biology, Royal Holloway/Bedford

New

College, Egham, Surrey TW20 0EX, United Kingdom SOURCE: Journal of Physiology, (1993) 467/- (107P).

ISSN: 0022-3751 CODEN: JPHYA7

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 002 Physiology 029 Clinical Biochemistry

LANGUAGE: English

L20 ANSWER 12 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 92253349 EMBASE

DOCUMENT NUMBER: 1992253349

TITLE: Lactoferrin uptake by the rat liver. Characterization of the recognition site and effect of selective modification

of arginine residues.

AUTHOR: Ziere G.J.; Van Dijk M.C.M.; Bijsterbosch M.K.; Van

Berkel

TIC

CORPORATE SOURCE: Division of Biopharmaceutics,

Bio-Pharmaceutical Sciences

Center, University of Leiden, P. O. Box 9503,2300 RA

Leiden, Netherlands

SOURCE: Journal of Biological Chemistry, (1992) 267/16

(11229-11235).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English SUMMARY LANGUAGE: English

AB Recently it was found that lactoferrin, an iron-binding glycoprotein with a molecular weight of 76,500, inhibits the remnant receptor-mediated uptake of apolipoprotein E (apoE)-bearing lipoproteins by the liver. In the present study we characterized the hepatic recognition of lactoferrin. Intravenously injected 1251-lactoferrin was cleared rapidly from the circulation by the liver (92.8 .+-. 9.5% of the dose at 5 min after injection). Parenchymal ***cells*** contained 97.1 .+-, 1.5% of the hepatic radioactivity. Internalization, monitored by measuring the release of liver-associated radioactivity by the polysaccharide fucoidin, occurred slowly. Only about 40% of the liver- associated lactoferrin was internalized at 10 min after injection, and it took 180 min to internalize 90%. Subcellular fractionation indicated that internalized lactoferrin is transported to the lysosomes. Binding of lactoferrin to isolated parenchymal liver ***cells*** was saturable with a dissociation constant of 10 .mu.M (20 x 106 binding sites/ ***cell***). The role of arginine residues on lactoferrin was studied by modifying these residues with 1,2-cyclohexanedione. The modification resulted in a strongly reduced

liver association (15.9.+-. 1.6% of the dose at 5 min after injection). Furthermore, unlabeled 1,2-cyclohexanedione-modified lactoferrin did not inhibit the binding of 1251-lactoferrin to isolated parenchymal ****cells***. Arginine residues on lactoferrin thus appear to be essential for its specific recognition by parenchymal liver ***cells***. In particular the clustered N- terminal arginine residues, which resemble the arginine-rich receptor binding sequence in apoE, may be responsible for both the interaction of lactoferrin with its recognition site and the inhibition of the hepatic uptake of apoE- bearing

lipoproteins.

L20 ANSWER 13 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 90208247 EMBASE
DOCUMENT NUMBER: 1990208247
TITLE: Organic solvent in intravenous fluids.
SOURCE: Lancet, (1990) 336/8706 (44).

ISSN: 0140-6736 CODEN: LANCAO

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal: Note

FILE SEGMENT: 007 Pediatrics and Pediatric Surgery

030 Pharmacology 037 Drug Literature Index

LANGUAGE: English

L20 ANSWER 14 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 84111485 EMBASE DOCUMENT NUMBER: 1984111485

TITLE: Identification of in vitro rat metabolites of

1-phenylcyclohexene.

AUTHOR: Cook C.E.; Brine D.R.; Tallent C.R.

CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle

Institute,

Research Triangle Park, NC 27709, United States

SOURCE: Drug Metabolism and Disposition, (1984) 12/2 (186-192).

CODEN: DMDSAI
COUNTRY: United States

COUNTRY: United States
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

030 Pharmacology

040 Drug Dependence, Alcohol Abuse and Alcoholism

024 Anesthesiology

LANGUAGE: English

AB In vitro metabolites of 1-phenylcyclohexene produced by the 10,000g supernatant fraction from rat liver homogenates were identified by a combination of spectrometric, chromatographic, and synthetic techniques. Initial oxidation occurred in the 3-position of 1-phenylcyclohexene to yield 1-phenyl-1-cyclohexen-3-one and 1-phenyl-1-cyclohexen-3-o1.

Further

allylic oxidation at the 6-position occurred to form 1-phenyl-6-hydroxy-1-cyclohexen-3-one and 1-phenyl-1-cyclohexene-3,6-diol.

Trans-1-phenyl-1-

cyclohexene-3,4-diol was also found and may have resulted from hydroxylation of 1-phenyl-1-cyclohexen-3-one .alpha. to the carbonyl to yield 4-hydroxy-1-phenyl-1-cyclohexen-3-one (not isolated) followed by carbonyl reduction. Oxidation of the double bond also occurred to give the cis and trans isomers of 1-phenylcyclohexane-1,2-diol as well as a compound postulated to be 1-phenylcyclohexane-1,2,3-triol.

L20 ANSWER 15 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI.

B.V.

ACCESSION NUMBER: 84088112 EMBASE

DOCUMENT NUMBER: 1984088112

TITLE: Binding of [3H]phencyclidine to rat and human blood constituents.

AUTHOR: Martin B.R.; Reynolds M.L.; Harris L.S.; Toro-Goyco E. CORPORATE SOURCE: Department of Pharmacology, Medical College of Virginia.

Virginia Commonwealth University, Richmond, VA 23298,

United States

SOURCE: Biochemical Pharmacology, (1984) 33/3 (429-434).

CODEN: BCPCA6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

040 Drug Dependence, Alcohol Abuse and Alcoholism

023 Nuclear Medicine

030 Pharmacology

LANGUAGE: English

AB The binding of (3H)phencyclidine (PCP) to rat serum and human plasma was

studied using equilibrium dialysis. [3H]PCP bound with a relatively low affinity to both rat serum $[K(D) = 1.5 \times 10-5 \text{ M}]$ and human plasma [K(D)

 $6.2 \times 10-6 M$). However, the binding capacity was quite large for rat serum

(5.7 nmoles/ml) and human plasma (5.6 nmoles/ml). Binding was readily reversible as shown by the efflux of [3H]PCP from a dialysis bag containing the rat serum-drug complex. In addition, the [3H]PCP-human serum complex appeared to dissociate completely when analyzed by Sephadex

gel filtration chromatography. The low affinity of PCP for serum appeared to account in large part for the high ***tissue*** -to-plasma ratios that are observed in animals and humans injected with this drug. In vitro equilibrium of [3H]PCP between rat serum and ***tissue*** homogenates

resulted in at least a 10-fold accumulation of [3H]PCP in the homogenates.

[3H]PCP was found to bind weakly to the major protein components of human

serum (macroglobulins, immunoglobulins and albumins). The weak nature of

the binding to serum proteins coupled with the relatively high capacity of binding probably account for the failure of other drugs to compete for PCP

L20 ANSWER 16 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 84044355 EMBASE

DOCUMENT NUMBER: 1984044355

TITLE: Mutagenicity of 3 structurally related epoxides, with defined stereochemical configuration, in Saccharomyces cerevisiae and in V79 Chinese hamster ***cells*** .

AUTHOR: Turchi G.; Bauer C.; Bronzetti G.; et al.

CORPORATE SOURCE: Istituto di Mutagenesi e Differenziamento, CNR, Pisa, Italy

SOURCE: Mutation Research, (1983) 117/1-2 (213-224).

CODEN: MUREAV COUNTRY: Netherlands DOCUMENT TYPE: Journal

FILE SEGMENT: 022 Human Genetics

Toxicology 052 004 Microbiology English

LANGUAGE: AB 3 Structurally related epoxides, 3,4-epoxycyclohexane,

trans-1,2,3,4-diepoxycyclohexane and trans-3,4-epoxycyclohexane-r-1,trans-

2-diol (anti isomer) were tested for their ability to induce both point mutation, mitotic gene conversion and recombination in a diploid strain (D7) of the yeast Saccharomyces cerevisiae, with and without a

mammalian microsomal activation system, and the formation of 6-thioguanine-resistant mutants in V79 hamster ***cells*** Genetic effects were related to the alkylating properties of the epoxides, as measured by alkylation of 4-(p-nitrobenzyl)pyridine (NBP). Of the 3 epoxides, only

3,4-epoxycyclohexane, characterized by the highest reactivity towards NBP,

induced all genetic effects in both test systems. A marginal activity was shown by trans-1,2,3,4-diepoxycyclohexane only in the yeast. The lack of genetic activity of the anti isomer of 3,4-epoxycyclohexane-1,2-diol, in spite of the formal similarity of its functional groups with those present in mutagenic polycyclic arene epoxydiols, was attributed to the dramatic reduction of lipophilicity of the molecule.

L20 ANSWER 17 OF 54 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 81221142 EMBASE DOCUMENT NUMBER: 1981221142

TITLE: Alkylating properties and genetic activity of 4-vinylcyclohexene metabolites and structurally related epoxides.

AUTHOR: Turchi G.; Bonatti S.; Citti L.; et al.

CORPORATE SOURCE: Ist. Mutagenesi Differenziam., CNR, Pisa, Italy SOURCE: Mutation Research, (1981) 83/3 (419-430).

CODEN: MUREAV

COUNTRY: Netherlands DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

022 Human Genetics

Occupational Health and Industrial Medicine 035

LANGUAGE: English

AB The mutagenicity of the epoxides 4-vinyl-1,2-epoxycyclohexane, 4-epoxyethyl-1,2-epoxycyclohexane,

4-epoxyethyl-1,2-dihydroxycyclohexane,

1,2-epoxycyclohexane and styrene oxide was assayed on the TA100 strain

S. typhimurium and V79 Chinese hamster ***cells*** . In the latter ***cell*** system, both point mutation (6-thioguanine resistance) and chromosomal damage (anaphase bridges and micronuclei) were scored.

effects were related to the alkylating properties of the epoxides. For this purpose, alkylation of 4-(p-nitrobenzyl)pyridine (NPB) and sodium-p-nitrothiophenolate (NTP) was measured and values for the substrate constant (s) were calculated.

4-Epoxyethyl-1,2-epoxycyclohexane,

1,2-epoxycyclohexane and styrene oxide, characterized by the highest activity toward NBP and by an s value in the vicinity of 1, were mutagenic in all test systems. 4-Vinyl-1,2-epoxycyclohexane and 4-epoxyethyl-1,2dihydroxycyclohexane, characterized by lower NBP reactivity and higher

value (1.30-1.38), did not induce reversion in S. typhimurium or 6-thioguanine-resistant mutants in V79 ***cells***, but were as effective as the 3 other compounds in the induction of chromosomal

L20 ANSWER 18 OF 54 MEDLINE

ACCESSION NUMBER: 90335219 MEDLINE

DOCUMENT NUMBER: 90335219 PubMed ID: 2165805

TITLE: Synthesis of affinity ligands and radioactive probes for isolation and study of myo-inositol 1,4,5-trisphosphate binding proteins.

AUTHOR: Jina A N; Ralph J; Ballou C E

CORPORATE SOURCE: Department of Biochemistry, University of California,

Berkeley 94720.

CONTRACT NUMBER: GM 35824 (NIGMS)

SOURCE: BIOCHEMISTRY, ***(1990 May 29)*** 29 (21) 5203-9.

Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English FILE SEGMENT:

Priority Journals ENTRY MONTH: 199009

ENTRY DATE: Entered STN: 19901012 Last Updated on STN: 19901012

Entered Medline: 19900911

AB To synthesize an affinity matrix for isolation of D-myo-inositol 1,4,5-trisphosphate binding proteins, racemic 3-cyclohexene-1carboxaldehyde was oxidized and converted to a mixture of trans-3,4-di-hydroxycyclohexane-1-carboxylic acid methyl ester isomers, which was phosphorylated and separated into (+-)-(1R,3R,4R)- and (+-)-(IR,3S,4S)-trans-3,4-bis[(diphenoxyphosphoryl)oxy]cyclohex an e-1carboxylic acid methyl esters. Each of these racemic compounds was hydrogenolyzed and reacted with ethylenediamine to give a monoamide, N-(2-aminoethyl)-bis(phosphonyloxy)cyclohexane-1-carboxamide, that

coupled to cyanogen bromide activated Sepharose 4B to provide the desired

affinity matrices. The intermediate trans-3,4-

bis[(diphenoxyphosphoryl)oxy]cyclohexane-1-carboxylic acid methyl

was also reduced with lithium borotritide to give the

(hydroxy[3H]methyl)cyclohexane derivative, which was phosphorylated

hydrogenolyzed to yield trans-3,4-bis(phosphonyloxy)-1-[(phosphonyloxy)[3H]methyl]cy clohexane, a radiolabeled analogue of inositol 1,4,5-trisphosphate. The carboxamide was also coupled to 4-azidosalicylic acid, and the product was iodinated to provide a 125I-radiolabeled photoactivatable cross-linking derivative of ***cyclohexanediol*** bisphosphate.

L20 ANSWER 19 OF 54 MEDLINE

ACCESSION NUMBER: 84008154 MEDLINE

DOCUMENT NUMBER: 84008154 PubMed ID: 6619130

The role of arginyl residues in estrogen receptor activation and transformation.

AUTHOR: Muller R E; Mrabet N T; Traish A M; Wotiz H H CONTRACT NUMBER: CA 28856 (NCI)

HD 15213 (NICHD)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, ***(1983 Oct 10)***

258 (19) 11582-9.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English FILE SEGMENT:

Priority Journals

ENTRY MONTH: 198311

ENTRY DATE: Entered STN: 19900319 Last Updated on STN: 19970203 Entered Medline: 19831123

AB Receptor-estradiol complexes (RE2) formed at 0 degree C in hypotonic buffers bind poorly to nuclei (nonactivated state); their sedimentation coefficient in low or high salt sucrose density gradients (SDG) is 8 S or 4 S, respectively (untransformed state); estradiol dissociates from untransformed RE2 at a high rate (k-1 = 0.44 min-1). Brief heating (28 degrees C, 30 min) induces activation (increased binding of RE2 to nuclei and polyanions), transformation (formation of receptor dimers which sediment at 6 S in 0.4 M KCl/borate SDG) and RE2 transition into a state from which E2 dissociates at a lower rate (k-2 = 8 X 10(-3) min-1). We have examined the role of arginyl residues in the above changes in receptor properties. It is well established (Patthy, L., and Smith, E. L. (1975) J. Biol. Chem. 250, 557-564; 565-569) that 1,2-cyclohexanedione (1,2-CHD) is a highly specific arginine-modifying agent; in borate buffer at 28 degrees C, but not at 0 degrees C, peptide arginyls are covalently modified. RE2 complexes heated in the presence of 1,2-CHD (50 mM)

poorly to nuclei; 1,4-cyclohexamedione and 1,2- ***cyclohexanediol*** had no effect. This reagent also prevents the temperature-induced transition of RE2 into a state with slow E2 dissociation rates although it does not interfere with heat transformation (formation of 6 S dimer). Modification of heat-activated and transformed RE2 by 1,2-CHD causes a loss in receptor binding to nuclei and alters RE2 from a state with slow into a state with fast E2 dissociation rates, although the receptor remains unaltered in the transformed 6 S state. At 0 degree C, i.e. in the absence of covalent arginyl modification, 1,2-CHD promotes dissociation of

the 8 S aggregate into 4.6 S subunits which bind to nuclei to the same extent as heat-transformed control RE2. Heating of the molybdate-stabilized 8 S receptor in the presence of 1,2-CHD yields a nonactivated 8 S receptor (4.6 S on high salt SDG); removal of molybdate and unreacted 1,2-CHD by gel filtration at 0 degree C followed by exposure

to high ionic strength causes 8 S to 4 S dissociation; these 4 S subunits, however, do not bind to nuclei, suggesting that their nucleotropic domain was accessible to 1,2-CHD modification while the receptor was in the aggregated 8 S state. It is proposed that the nuclear binding site of the estrogen receptor contains arginyl residues. Furthermore, a distinct set of arginyl residues appears to be related to the estrogen-binding domain; its integrity is required for the heat-induced formation and maintenance of the RE2 state with slow E2 dissociation.(ABSTRACT TRUNCATED AT 400

WORDS)

L20 ANSWER 20 OF 54 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1999-571686 [48] WPIDS

C1999-166775 DOC. NO. CPI: TITLE:

Formation of amyloid plaques using amyloid protein and sulfated macromolecules, for, e.g. identification of agents for treating Alzheimer's disease.

DERWENT CLASS: A14 A96 B04 C07 D16 CASTILLO, G; SNOW, A D INVENTOR(S): PATENT ASSIGNEE(S): (UNIW) UNIV WASHINGTON COUNTRY COUNT: PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 9945947 A1 19990916 (199948)* EN 89 <--RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD

GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR

MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT

UA UG UZ VN YU ZW

AU 9930838 A 19990927 (200006) EP 1064013 A1 20010103 (200102) EN R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT RO SE

123

APPLICATION DETAILS:

JP 2002506043 W 20020226 (200219)

PATENT NO KIND APPLICATION DATE WO 9945947 A1 WO 1999-US5438 19990312 AU 9930838 A AU 1999-30838 19990312 EP 1999-912468 19990312 EP 1064013 A1 WO 1999-US5438 19990312 JP 2002506043 W WO 1999-US5438 19990312 JP 2000-535360 19990312

FILING DETAILS:

PATENT NO KIND PATENT NO AU 9930838 A Based on WO 9945947 EP 1064013 Al Based on JP 2002506043 W Based on WO 9945947 WO 9945947

PRIORITY APPLN. INFO: US 1998-77924P 19980313 AN 1999-571686 [48] WPIDS

AB WO 9945947 A UPAB: 19991122

NOVELTY - Formation of amyloid plaques by co-incubation of an amyloid

protein (AP) with sulfated macromolecules is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following:

- (1) identification of anti-amyloid plaque therapeutics comprising:
- (a) labeling AP or sulfated macromolecules;
- (b) forming amyloid plaques in vitro from the labeled AP following incubation in distilled water or Tris-buffered saline (pH 7.0-7.4) at 37 deg. C for 7 days;
- (c) adding a known amount of potential plaque therapeutic for a given time, and
 - (d) detecting breakdown or disruption of the amyloid plaques;
- (2) an in vivo assay for selecting a candidate therapeutic for inhibiting or disrupting amyloid plaque deposition or persistence comprising:
- (a) pre-forming congophilic maltese-cross amyloid plauqes in vitro following incubation of an AP and a selected sulfated macromolecule;
- (b) using a first cannula and osmotic pump to continuously infuse, for a selected duration, the pre-formed congophilic maltese-cross amyloid plaques into a ***tissue*** or organ;
- (c) changing the first cannulae and osmotic pump with a second cannulae and osmotic pump to administer the candidate therapeutic; and
- (d) detecting the candidate therapeutic's ability to disrupt, reduce, or eliminate congophilic maltese-cross amyloid plaque deposition/persistence in the ***tissue*** or organ.

USE - The methods can be used to study the formation of amyloid plaques and to identify anti-plaque therapeutics. They can be used for diseases such as Alzheimer's disease, Cretzfeldt-Jakob disease, Gerstmann-Straussler syndrome and kuru.

Dwg.0/7

L20 ANSWER 21 OF 54 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1999-540548 [45] WPIDS

C1999-157843 DOC. NO. CPI:

New ***cyclohexanediol*** derivatives for treatment TITLE: of hyperproliferative skin diseases - such as psoriasis, basal ***cell*** carcinoma, keratosis and keratinization.

DERWENT CLASS:

INVENTOR(S): BARBIER, P; BAUER, F; MOHR, P; MUELLER, M; PIRSON, W;

MULLER, M

PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) HOFFMANN LA

ROCHE INC COUNTRY COUNT: PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

seborrheic dermatitis or for reversing conditions associated with WO 9943646 A1 19990902 (199945)* EN 40 <-photodamage, particularly treatment of skin damaged through sun RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE exposure, LS LU MC MW NL the effects of wrinkling, elastosis and premature aging. OA PT SD SE SZ UG ZW Dwg.0/0 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE L20 ANSWER 22 OF 54 WPIDS (C) 2002 THOMSON DERWENT DK EE ES FI GB GD ACCESSION NUMBER: 1999-277604 [23] WPIDS GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV CROSS REFERENCE: 2001-015701 [63] MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK DOC. NO. CPI: C1999-081639 Preparing a polyester polyol based resin blend for rigid closed ***cell*** foam. SL TJ TM TR TT TITLE: UA UG UZ VN YU ZW ZA 9901550 A 19991124 (200001) DERWENT CLASS: A25 A26 A32 A60 A94 39 <--AU 9926246 A 19990915 (200004) INVENTOR(S): HICKEY, FL BR 9908315 A 20001107 (200063) PATENT ASSIGNEE(S): (STEP) STEPAN CO EP 1056716 A1 20001206 (200064) EN COUNTRY COUNT: R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU NL PT SE PATENT INFORMATION: US 6184422 B1 20010206 (200109) CN 1291974 A 20010418 (200141) PATENT NO KIND DATE WEEK LA PG KR 2001041313 A 20010515 (200167) MX 2000008236 A1 20010301 (200170) WO 9919377 A1 19990422 (199923)* EN 41 <--JP 2002504537 W 20020212 (200215) RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL APPLICATION DETAILS: OA PT SD SE SZ UG ZW W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE PATENT NO KIND APPLICATION DATE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT WO 9943646 A1 WO 1999-EP1118 19990220 LU LV MD MG ZA 9901550 A ZA 1999-1550 19990225 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ AU 1999-26246 19990220 AU 9926246 A TM TR TT UA UG BR 9908315 A BR 1999-8315 19990220 US UZ VN YU ZW WO 1999-EP1118 19990220 US 5922779 A 19990713 (199934) EP 1056716 A1 EP 1999-906250 19990220 AU 9896877 A 19990503 (199937) WO 1999-EP1118 19990220 EP 1023351 AI 20000802 (200038) EN US 6184422 B1 US 1999-252508 19990218 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV CN 1291974 A CN 1999-803314 19990220 MC MK NL PT KR 2001041313 A KR 2000-709419 20000825 RO SE SI MX 2000008236 A1 MX 2000-8236 20000823 EP 1023351 B1 20020327 (200222) EN JP 2002504537 W WO 1999-EP1118 19990220 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT JP 2000-533405 19990220 RO SE SI FILING DETAILS: MX 2000003503 AI 20010601 (200235) DE 69804483 E 20020502 (200237) PATENT NO PATENT NO KIND APPLICATION DETAILS: WO 9943646 AU 9926246 A Based on WO 9943646 BR 9908315 A Based on PATENT NO KIND APPLICATION DATE EP 1056716 A1 Based on WO 9943646 JP 2002504537 W Based on WO 9919377 A1 WO 1998-US21077 19981007 WO 9943646 US 1997-949239 19971010 US 5922779 A PRIORITY APPLN. INFO: EP 1998-103346 19980226 AU 9896877 A AU 1998-96877 19981007 AN 1999-540548 [45] WPIDS EP 1023351 A1 EP 1998-950968 19981007 AB WO 9943646 A UPAB: 19991103 WO 1998-US21077 19981007 NOVELTY - New ***cyclohexanediol*** derivatives are prepared by EP 1023351 B1 EP 1998-950968 19981007 cleaving the protecting groups Y', Z' and R4 from (II) in the presence of WO 1998-US21077 19981007 tetrabutylammonium fluoride in an inert solvent.

DETAILED DESCRIPTION - ***Cyclohexanediol*** derivatives MX 2000003503 A1 MX 2000-3503 20000410 DE 69804483 E DE 1998-604483 19981007 οf EP 1998-950968 19981007 formula (1) are new: WO 1998-US21077 19981007 X = C = CH2 or CH2; Y, Z = H, F or OH;FILING DETAILS: A = C triple bond C, CH=CH or CH2CH2; R1, R2 = alkyl or perfluoroalkyl; PATENT NO KIND PATENT NO R3 = lower alkyl An INDEPENDENT CLAIM is included for intermediate protected AU 9896877 A Based on WO 9919377 EP 1023351 A1 Based on WO 9919377 compounds of formula (II): EP 1023351 BI Based on WO 9919377 Y', Z' = protected OH;DE 69804483 E Based on EP 1023351 R4 = OH protecting group WO 9919377 Based on

ACTIVITY - Antiproliferative agent;

4-280 nM; calcitriol ED50 2.8 nM)

Application of (I)

MECHANISM OF ACTION - Vitamin-D receptor agonist.

neoplastic diseases, disorders of the sebaceous glands such as acne and

resulted in upto a 10-fold increase in vitamin-D receptor activation (ED50 CR 2001-015701 [63] AB WO 9919377 A UPAB: 20020613 USE - (I) are antiproliferative agents useful for treatment or NOVELTY - Preparing rigid closed ***cell*** polyisocyanate-based prevention of hyperproliferative skin diseases particularly psoriasis, basal ***cell*** carcinomas, keratinization disorders and keratosis, comprising polyol resin blends having increased phase stability and lower

AN 1999-277604 [23] WPIDS

viscosity.

PRIORITY APPLN. INFO: US 1997-949239 19971010

DETAILED DESCRIPTION - A method for preparing a rigid closed ***cell*** polyisocyanate-based foam comprises reacting an organic aromatic polyisocyanate and a polyol in the presence of a nonionic surfactant and a 4-7C aliphatic or cycloaliphatic hydrocarbon blowing agent. The polyol resin blend comprising an aromatic polyester polyol formed by inter-esterification reaction between: (i) a phthalic acid based material; (ii) a hydroxylated material having a functionality of at least 2; and (iii) a hydrophobic material having: (I) from 1-6 radicals selected from carboxylic acid (ester) groups, hydroxyl groups and their mixtures; and (II) hydrocarbon groups comprising a total of at least 4C atoms for each radical present in the hydrophobic material; and (III) an average molecular weight from 100-1000.

An INDEPENDENT CLAIM is also included for a polyester polyol based

resin blend.

USE - Used to make rigid closed ***cell*** polyisocyanate-based foams which are dimensionally stable, have good insulation values and excellent flame retardance.

ADVANTAGE - Have increased phase stability and lower viscosity. Dwg.0/0

L20 ANSWER 23 OF 54 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1999-277259 [23] WPIDS

DOC. NO. NON-CPI: N1999-207828

DOC. NO. CPI: C1999-081438

Use of ice-controlling molecules comprising an aliphatic TITLE: moiety bearing 2 or more substituents that simultaneously form hydrogen bonds with ice.

DERWENT CLASS: A60 A83 A95 B04 C03 D13 D15 D22 E15 E17

P13

INVENTOR(S): FAHY, G M

PATENT ASSIGNEE(S): (LIFE-N) LIFE SCI HOLDINGS INC;

(ORGA-N) ORGAN INC

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 9918169 A1 19990415 (199923)* EN 63 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE

GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG

MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG

UZ VN YU ZW

AU 9897842 A 19990427 (199936) EP 1019458 A1 20000719 (200036) EN

R: CH DE FR GB LI

APPLICATION DETAILS:

PATENT NO	KINI	D APPLICATION DATE
WO 9918169	Αl	WO 1998-US20834 19981002
AU 9897842	Α	AU 1998-97842 19981002
EP 1019458	A1	EP 1998-952047 19981002
		WO 1998-US20834 19981002

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9897842	A Based on	WO 9918169
EP 1019458	A1 Based on	WO 9918169

PRIORITY APPLN. INFO: US 1997-943147 19971003

AN 1999-277259 [23] WPIDS

AB WO 9918169 A UPAB: 20011203

NOVELTY - Molecules comprising an aliphatic moiety bearing 2 or more substituents that simultaneously form hydrogen bonds with ice are used for promoting nucleation of ice crystals, inhibiting growth of ice crystals, or bonding a material to ice

USE - Ice crystal growth can be inhibited in an ice crystal, a

cryoprotective solution, a food product, a living plant, a vehicle

surface, a road surface, a walkway, a light transmitter or a utility line; in an organ, body fluid or other body ***tissue*** or ***cell*** that is to be cooled for ***cryopreservation***; or a solid coated with a thin layer of ice.

The compounds are useful in bonding a material such as tire treads and shoes to ice, to reduce accidents; and for promoting nucleation of ice crystals in clouds. Dwg.0/19

L20 ANSWER 24 OF 54 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1991-339538 [46] WPIDS

CROSS REFERENCE: 1990-099248 [13] DOC. NO. CPI: C1991-146537

· TITLE: New mitomycin derivs. having reduced bone marrow

toxicity

- used for treating bacterial infection caused by e.g. Escherichia, and cancer, e.g. leukaemia and melanoma.

DERWENT CLASS: B02 C01 C02 D22 E19

CLARKE, R R; GHIORGHIS, A; TALEBIAN, A INVENTOR(S):

PATENT ASSIGNEE(S): (GEOU) UNIV GEORGETOWN

COUNTRY COUNT: PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 9116049 A 19911031 (199146)* RW: AT BE CH DE DK ES FR GB GR IT LU NL SE W: AU CA JP AU 9177923 A 19911111 (199207) <--US 5091523 A 19920225 (199211) 32 <--EP 533692 A1 19930331 (199313) EN 85 <--R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE JP 06500532 W 19940120 (199408) NZ 237941 A 19940225 (199411) AU 656137 B 19950127 (199512) EP 533692 A4 19950322 (199612)

APPLICATION DETAILS:

PATENT NO	KIN	D APPLICATION DATE
US 5091523	Α	US 1990-620853 19901203
EP 533692	Αl	EP 1991-909073 19910425
		WO 1991-US2850 19910425
JP 06500532	W	JP 1991-508867 19910425
		WO 1991-US2850 19910425
NZ 237941	Α	NZ 1991-237941 19910424
AU 656137	В	AU 1991-77923 19910425
EP 533692	A4	EP 1991-909073

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 533692	Al Based on	WO 9116049
JP 06500532	W Based on	WO 9116049
AU 656137	B Previous Pub	ol. AU 9177923
Ra	sed on WO	9116049

PRIORITY APPLN. INFO: US 1990-513266 19900425; US 1990-620853

AN 1991-339538 [46] WPIDS

CR 1990-099248 [13]

AB WO 9116049 A UPAB: 19940928

Mitomycin derivatives of formula (I) are new. R = H or 1-4C alkyl. A = 1-4C alkylene or unsaturated alkylene, phenylene (opt. substd.), benzylene (opt. substd.), heteroaryl (opt. substd.) or 3-6C heterocycloalkyl. n,n1 = 0 or 1. A1 = 0, 1-4C opt. saturated alkylene, -CO-NH- or -NH-CO-, A2 =

0, 1-4C opt. saturated alkylene, NH, NR or -NH-CO-. n2 = 0 or 1. Y = glucopyranosyl, galactopyranosyl, mannopyranosyl, xylopyranosyl, cellobiosyl, lactosyl, glucosuranosyl, maltosyl or 1,3-

cyclohexanediol -2-yl, their hydroxyl protected derivs. or the corresponding amino-, diamino- or triaminosaccharides. Provided that

n is 1, then A1 is 1-4C opt. saturated alkylene, and when n is 0, then 1 or n1 and n2 is O. 6 compounds are specifically claimed including 7-(3-(2-acetamido-3,4,6-tri-O-acetyl -beta-D-glucopyranosyl)-amino)

carbonylpropylamino)-9-methoxymitosane.

Also claimed are mitomycin derivatives of formulae (II) and (III). Al = A. Q1, Q2, Qa, Qb = independently Y or a group of formula H-(NH-CH(R1)-CO)-q. Rl = H or 1-4C alkyl (opt, susbtd.). q = 0-4. USE/ADVANTAGE - For treating bacterial infection (claimed), preferably caused by Escherichia, Pseudomonas, Salmonella, Staphylococcus,

Klebsiella and Listeria, and for treating cancer (claimed) by suppressing growth of cancer ***cells*** . The cancer is preferably leukaemia, melanoma, sar

ABEQ US 5091523 A UPAB: 19930928

Mitomycin derivs, of formulae (1)-(V1) are new. In these, n, n1, n2 and 0 or 1; q is 0-4; Y is gluco- galacto-, manno- or xylo-pyranosyl, cellobiosyl, lactosyl, glucofuranosyl maltosyl, or 2-amino-1,3-

cyclohexanediol , or their OH-protected acetate derivs.; R is H; R1

is H, 1-4C alkyl opt. substd., 1-4C alkylthio, OH, COO, NH2, guanidino, imidazole, or carbamoyl; or R1 and R2 form 5- or 6-membered N-contg.

R2 is NH2 or MeO; R3 is 3-cyano-4-morpholinyl-2-deoxypyranosyl saccharide

opt. without the 3-CN gp.; A is 1-4C alkylene or unsatd. alkylene, phenylene, benzylene, heteroaryl, all opt. substd. or 3-6C heteroaryl-alkyl; A1 is O, 1-4C alkylene, NH, NR or NHCO; Qa and Qb

alkali metal or as Y or corresp. mono-, di- and tri-aminosaccharides or (a).

A typical cpd. is N7-(2-deoxyglucopyranosyl)mitomycin C. A typical prepn. is by dehydration-condensing an N-protected amino acid with an alcohol to activated ester and condensing this with an amino cpd., deprotecting the conjugate and condensing with mitomycin A or C.

USE - The treatment of bacterial infections and to suppress growth of cancer ***cells*** . Topical dose is 0.01-1000 mcg/ml.

L20 ANSWER 25 OF 54 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1988-362747 [51] WPIDS DOC, NO, CPI: C1988-160440

TITLE: Compsns. for treating chronic viral infections - contg. sterile aq. beta-glucuronidase soln. 1,3-cyclohexan di ol and protamine.

DERWENT CLASS: B04 D16
PATENT ASSIGNEE(S): (MCEW-I) MCEWAN L M
COUNTRY COUNT: 2

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

GB 2205746 A 19881221 (198851)* 11 <-GB 2205746 B 19910327 (199113) <-IT 1218080 B 19900412 (199210) <--

APPLICATION DETAILS:

PATENT NO KIND APPLICATION DATE

GB 2205746 A GB 1988-14195 19880615

PRIORITY APPLN. INFO: GB 1987-13906 19870615 AN 1988-362747 [51] WPIDS

AB GB 2205746 A UPAB: 19930923

Compsns. for treating post viral syndrome or AIDS comprise a sterile aq. soln. of highly purified beta-glucuronidase (I).

The soln. pref. contains 50-1000 FU of (1) per dose, esp. together with 10 power -11 - 10 power -7 g of 1,3-***cyclohexanediol*** (11) and 10 power -8 - 10 power -5 g of protamine (111), in a sterile phosphate-free buffer soln. The soln. may be administered together with

antigen, e.g. food allergen.

ADVANTAGE - (I) stimulates immune response to chronic viral infections, e.g. by increasing T4 helper ***cell*** counts in HIV infections. 0/0

ABEQ GB 2205746 B UPAB: 19930923

The use of beta-glucuronidase for the manufacture of a composition for

in the treatment of post viral syndrome which composition comprises a sterile aqueous solution of beta-glucuronidase.

L20 ANSWER 26 OF 54 WPIDS (C) 2002 THOMSON DERWENT ACCESSION NUMBER: 1978-50045A [28] WPIDS

TITLE: Sublimable compsns. contg. hydrocarbon and polar cpd. -

are used to release e.g. perfumes, insecticides, deodorants, rust and mould inhibitors and
preservatives into atmos..

DERWENT CLASS: C03 G04 P24 P34
INVENTOR(S): HAYASHI, H; ICHIKAWA, H; SATO, H
PATENT ASSIGNEE(S): (IDEK) IDEMITSU IND CO LTD

COUNTRY COUNT: 5 PATENT INFORMATION:

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PATENT NO KIND DATE WEEK LA PG
DE 2756953 A 19780706 (197828)*
JP 53081630 A 19780719 (197834)
JP 53081632 A 19780719 (197834)
FR 2375310 A 19780825 (197839)
                                   JP 53121936 A 19781024 (197848)
JP 53144476 A 19781215 (197905)
JP 53145920 A 19781219 (197905)
JP 53146975 A 19781221 (197906)
JP 54002349 A 19790109 (197907)
JP 54036211 B 19791108 (197949)
JP 55030989 B 19800814 (198037)
JP 55035175 B 19800911 (198041)
US 4233161 A 19801111 (198048)
JP 55049097 B 19801209 (198102)
JP 56008801 B 19810225 (198112)
JP 56014704 B 19810406 (198118)
GB 1594248 A 19810730 (198131)
                                    <--
JP 57048047 B 19821014 (198245)
DE 2756953 C 19830421 (198317)
```

PRIORITY APPLN. INFO: JP 1976-155650 19761225; JP 1976-155652 19761225; JP 1977-34674 19770330; JP 1977-58220 19770521; JP 1977-59360 19770524; JP 1977-61255 19770527; JP 1977-66298 19770607; JP 1977-123460 19771017

AN 1978-50045A [28] WPIDS

AB DE 2756953 A UPAB: 19930901

Sublimable compsus. contain ≥ 1 sublimable hydrocarbon and ≥ 1 sublimable

polar cpd. The hydrocarbon is pref. adamantane (I) endo-trimethylenenorbornane (II), cyclododecane, norbornane, trimethylborbornane and/or naphthalene. The polar cpd. is pref. dimethyl fumarate (III) benzoic acid, trioxymethylene, coumarin, p-dichlorobenzene, caprolactam, 1,4-***cyclohexanediol*** phthalide, lactide acid and/or triisopropyltrioxane.

The compsns. can be used to release active substances (perfumes, moth-proofing agents, insecticides, insect repellants or attractants, deodorants, rust inhibitors mould inhibitors, ***preservatives*** etc.) into the atmos. The polar cpds. retards the release of the active substance.

L20 ANSWER 27 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:671048 HCAPLUS

DOCUMENT NUMBER: 131:286669

TITLE: preparation of a dodecenylidenecyclohexanediol derivative to treat or prevent hyperproliferative skin diseases

INVENTOR(S): Bauer, Franz; Courtney, Lawrence F. PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., USA

SOURCE: U.S., 6 pp. CODEN: USXXAM

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 5969190 A 19991019 US 1998-79656 19980515 <--ZA 9804176 A 19990108 ZA 1998-4176 19980518 <--PRIORITY APPLN. INFO.: EP 1997-108355 A 19970523

OTHER SOURCE(S): MARPAT 131:286669

/ Structure 1 in file .gra /

AB The compd., (E)-(1R,3R)-5-[(R)-11-hydroxy-7,11-dimethyldodec-2enylidene]cyclohexane-1,3-diol (I) was prepd. Thus I was prepd. via the reaction of II prepd. from (-)-citronellal and III followed by the deprotection of silyl groups. I was formulated into soft gel capsules for oral administration or topical cream. I is useful in the treatment or prevention of hyperproliferative skin diseases, particularly psoriasis, basal ***cell*** carcinomas, disorders of keratinization and keratosis; or for reversing the conditions assocd, with photodamage. REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L20 ANSWER 28 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:222724 HCAPLUS

DOCUMENT NUMBER: 131:39206

TITLE: Chicoric Acid Analogs as HIV-1 Integrase Inhibitors AUTHOR(S): Lin, Zhaiwei; Neamati, Nouri; Zhao, He; Kiryu,

Yoshimitsu; Turpin, Jim A.; Aberham, Claudia; Strebel, Klaus; Kohn, Kurt; Witvrouw, Myriam; Pannecouque, Christophe; Debyser, Zeger; De Clercq, Erik; Rice, William G.; Pommier, Yves; Burke, Terrence R., Jr.

CORPORATE SOURCE: Laboratory of Medicinal Chemistry Division

of Basic

Sciences, National Cancer Institute, Bethesda, MD,

20892, USA

SOURCE: Journal of Medicinal Chemistry (***1999***),

42(8), 1401-1414

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal English

LANGUAGE:

AB The present study was undertaken to examine structural features of L-chicoric acid which are important for potency against purified HIV-1 integrase and for reported cytoprotective effects in ***cell*** -based systems. Through a progressive series of analogs, it was shown that enantiomeric D-chicoric acid retains inhibitory potency against purified

integrase equal to its L-counterpart and further that removal of either one or both carboxylic functionalities results in essentially no loss of inhibitory potency. Addnl., while two caffeoyl moieties are required, attachment of caffeoyl groups to the central linking structure can be

achieved via amide or mixed amide/ester linkages. More remarkable is

finding that blockage of the catechol functionality through conversion to tetraacetate esters results in almost no loss of potency, contingent on the presence of at least one carboxyl group on the central linker. Taken as a whole, the work has resulted in the identification of new integrase inhibitors which may be regarded as bis-caffeoyl derivs. of glycidic acid and amino acids such as serine and .beta.-aminoalanine. The present

also examd, the reported ability of chicoric acid to exert cytoprotective effects in HIV-infected ***cells*** . It was demonstrated in target and ***cell*** -based assays that the chicoric acids do not significantly inhibit other targets assocd. with HIV-1 replication, including reverse transcription, protease function, NCp7 zinc finger function, or replication of virus from latently infected ***cells*** In CEM ***cells***, for both the parent chicoric acid and selected analogs, antiviral activity was observable under specific assay conditions and with high dependence on the multiplicity of viral infection. However, against HIV-1- and HIV-2-infected MT-4 ***cells***, the chicoric

acids

and their tetraacetylated esters exhibited antiviral activity (50% effective concn. (EC50) ranging from 1.7 to 20 .mu.M and 50% inhibitory conen. (IC50) ranging from 40 to 60 .mu.M).

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L20 ANSWER 29 OF 54 HCAPLUS COPYRIGHT 2002 ACS 1999:161265 HCAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER: 130:201358

TITLE: Immobilized cobalt-salen complexes in zeolites as

catalysts for cyclohexene oxidation

AUTHOR(S): Ernst, Stefan; Weber, Astrid, Weichert, Joerg CORPORÀTE SOURCE: Fachbereich Chemie-Technische Chemie,

Universitaet

Kaiserslautern, Kaiserslautern, D-67653, Germany SOURCE: Chemie-Ingenieur-Technik (***1999***), 71(1/2),

CODEN: CITEAH; ISSN: 0009-286X

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal LANGUAGE:

AB Co-salen complexes [salen: N,N'-bis(salicyliden)ethylendiamin] were incorporated into the intercryst, cavities of zeolite NaY using the flexible ligand method. The complex content was adjusted to one

in every 2nd, 10th, and 20th unit ***cell*** of zeolite Y. The obtained host/guest compds. showed catalytic activity in the liq.-phase oxidn. of cyclohexene with aq. H2O2 (reaction products: I,2-

cyclohexanediol, 2-cyclohexenol, 2-cyclohexenone). For the 3 investigated complex concns., the catalytic activity per active center was independent from the complex content of the zeolite. The catalytic activity decreased only if the complex content was increased to 1 complex and 2 complexes per unit ***cell***, resp. (no data).

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES

AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L20 ANSWER 30 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:809975 HCAPLUS

DOCUMENT NUMBER: 130:217714

TITLE: Antisense oligonucleotides as anticancer agents

AUTHOR(S): Herdewijn, P.; Saison-Behmoaras, E.; Van Aerschot,

A.;

Leserman, L.; Eritja, R.; Pfleiderer, W.

CORPORATE SOURCE: Katholieke Universiteit Leuven, Louvain,

Belg.

SOURCE: Biomedical and Health Research (***1998***),

24(Cancer Research Supported under BIOMED 1), 182-189

CODEN: BIHREN; ISSN: 0929-6743

PUBLISHER: IOS Press DOCUMENT TYPE: Journal LANGUAGE: English

AB Antisense oligonucleotides were developed with in vivo antitumoral activity. The ***cellular*** model which was selected for the study of the biol. activity of the modified oligonucleotides consists of a stable clone of the human mammary ***cell*** line HBL 100 transformed

with Ha-ras DNA from a human bladder carcinoma ***cell*** line carrying a point mutation in codon 12. Optimization of the structure of oligonucleotides by chem, derivatization led to an antisense construct which inhibits ***cell*** growth at concn. (50 nM) which is 400 times lower than the concn. necessary for the unmodified antisense oligonucleotide to exert the same effect. In vivo studies in nude mice with local s.c. injections of the selected antisense oligonucleotide at the site of tumor growth confirmed the selective antisense effect which warrants further development of these constructs as antitumoral drugs. REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES

AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L20 ANSWER 31 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:794980 HCAPLUS

DOCUMENT NUMBER: 130:24804

TITLE: Preparation of ***cyclohexanediol*** derivatives

for use in the treatment or prevention of

hyperproliferative skin diseases

INVENTOR(S): Bauer, Franz; Courtney, Lawrence F.

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

PCT Int. Appl., 17 pp. SOURCE:

CODEN: PIXXD2 DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9852894 A1 19981126 WO 1998-EP2762 19980512 <--W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,

EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,

UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK. ES.

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9876539 A1 19981211 AU 1998-76539 19980512 <--EP 983221 A1 20000308 EP 1998-924303 19980512

EP 983221 B1 20020403 R: DE, ES, FR, GB, IT

JP 2000512315 T2 20000919 JP 1998-549892 19980512

JP 3276375 B2 20020422

PRIORITY APPLN. INFO.: EP 1997-108355 A 19970523

WO 1998-EP2762 W 19980512

OTHER SOURCE(S): MARPAT 130:24804

/ Structure 2 in file .gra /

AB Cyclohexane-1,3-diol I was prepd. and formulated for use in the treatment

or prevention of hyperproliferative skin diseases, particularly psoriasis, basal ***cell*** carcinomas, disorders of keratinization and keratosis, and for reversing the conditions assocd, with photodamage. Thus, I was prepd. starting from [2-[(3R,5R)-3,5-bis[[(1,1dimethylethyl)dimethylsilyl]oxy]cyclohexylidene]ethyl]diphenylphosphine oxide, (-)-citronellal, and tri-Et phosphonoacetate. Formulations for both oral and topical application were presented.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES **AVAILABLE FOR THIS**

RECORD. ALL CITATIONS AVAILABLE IN THE RE

L20 ANSWER 32 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:371582 HCAPLUS

DOCUMENT NUMBER: 129:130861

TITLE: Phase I and pharmacokinetic study of D-limonene in patients with advanced cancer

AUTHOR(S): Vigushin, David M.; Poon, Grace K.; Boddy, Alan; English, Jacqueline; Halbert, Gavin W.; Pagonis,

Christos: Jarman, Michael: Coombes, R. Charles CORPORATE SOURCE: Department Medical Oncology, Cancer Research Campaign

Laboratories, Charing Cross Hospital, London, W6 8RF,

SOURCE: Cancer Chemotherapy and Pharmacology (***1998***),

42(2), 111-117

CODEN: CCPHDZ; ISSN: 0344-5704

PUBLISHER: Springer-Verlag DOCUMENT TYPE: Journal LANGUAGE: English

AB Patients with refractory solid tumors completed 99 courses of D-limonene

0.5-12 g/m2/day administered orally in 21-day cycles. Pharmacokinetics were analyzed by liq. chromatog./mass spectrometry. Breast cancer patients received 15 cycles of D-limonene at 8 g/m2/day. Intratumoral monoterpene levels were measured in 20% of the breast cancer patients (2/10). The max. tolerated dose was 8 g/m2/day; nausea, vomiting, and diarrhea were dose limiting. One partial response in a breast cancer patient on 8 g/m2/day was maintained for 11 mo; 3 addnl. patients with colorectal carcinoma had prolonged stable disease. There were no responses in the phase II study. Peak blood plasma conen. (Cmax) for

D-limonene was 10.8-20.5 .mu.M. Predominant circulating metabolites were

perillic acid (Cmax 20.7-71), dihydroperillic acid (16.6-28.1), limonene-1,2-diol (10.1-20.7), uroterpenol (14.3-45.1 .mu.M), and an isomer of perillic acid. Both isomers of perillic acid, and cis and trans isomers of dihydroperillic acid were in urine hydrolates. Intratumoral levels of D-limonene and uroterpenol exceeded the corresponding plasma levels. Other metabolites were trace constituents in ***tissue*** D-Limonene was well tolerated in cancer patients at doses which were supposed to have clin, activity,

L20 ANSWER 33 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:108138 HCAPLUS

DOCUMENT NUMBER: 128:192879

TITLE: Preparation of dimerized glucose or glucosamine derivatives as ***cell*** adhesion inhibitors

Yuri, Masatoshi; Miyauchi, Hiroshi; Hayashi, Shoji; INVENTOR(S):

Tanaka, Masashi PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp. CODEN: JKXXAF

DOCUMENT TYPE: Patent LANGUAGE: Jananese FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

A2 19980217-JP 10045793 JP 1996-216839 19960729 <--OTHER SOURCE(S): MARPAT 128:192879

Gi

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB (MAB)2X or [MA(BD)n]2X [M = Q1; R0 = H, OH, substituted amino; 1 of R2-R3

= .alpha.- or .beta.-L-fucopyranosyl; another = O2; R4 = H. SO3H. PO3H2.

CH2CO2H, Q3; R5 = Me, CH2OH; B = C1-15 divalent group; A, D = O, CO2, NR6,

CONR6, NR6CO2, NR6CONR6, NR6C(S)O, NR6C(S)NR6; R6 = H, Me, Et, benzyl, Pr,

Ac, benzoyl; X = divalent ring; n = 1-10] or their salts, useful for treatment of inflammation, reperfusion injury, autoimmune diseases, and cancer metastasis, are prepd. Glucosamine deriv. Q4-Cl (R = Ac, R7 = Me)

(prepn. given, 1.26 g) was treated with 80 mg 1,3-bis(3-

hydroxypropyloxy)benzene (I; R8 = H) in CICH2CH2Cl in the presence of mol.

sieve 4A, Me2NCONMe2, and (CF3SO3)2Sn at room temp. for 12 h to give 578

mg ether, which was treated with MeONa in MeOH at room temp. for 36 h to

give 82% I.2Na (R8 = .beta.-Q4, R = R7 = H) (II). II inhibited adhesion of rsE-selectin with HL-60 ***cells*** with IC50 of 0.037 mM, vs. 0.20

mM, for monomeric glucosamine deriv.

L20 ANSWER 34 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:784513 HCAPLUS

DOCUMENT NUMBER: 128:94807

TITLE: Sensitivity Enhancement of Exciton Coupling by Fluorescence Detected Circular Dichroism (FDCD)

Dong, Jian-Guo; Wada, Akio; Takakuwa, Takashi; AUTHOR(S):

Nakanishi, Koji; Berova, Nina

CORPORATE SOURCE: Department of Chemistry, Columbia

University, New

York, NY, 10027, USA

SOURCE: Journal of the American Chemical Society (***1997***

), 119(49), 12024-12025

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE:

LANGUAGE: English

AB Exciton coupled CD characterized by split Cotton effects (couplets) is a nonempirical microscale method for detg. the abs. configurations or conformations of a wide variety of compds. The use of strongly absorbing and fluorescent chromophores enhances the CD sensitivity and enables handling of ng.apprx..mu.g scale material. Under favorable conditions, attachment of a prototype fluorescence detector to a regular JASCO-720 CD

spectropolarimeter leads to a 50-100-fold sensitivity enhancement over conventional CD measurements to exciton split bisignate couplets. The enhanced sensitivity of FDCD was demonstrated with 1(S),2(S)-trans-***cyclohexanediol*** bis-(6-methoxy-2-naphthoate) (1), 1(R),2(R)-trans-

cyclohexanediol bis(2-naphthoate) (2), a steroidal 3.beta., 6.alpha.-bis-(2-anthroate) (3), and ouabagenin 1,3,19-tris-(2-naphthoate) (4), with fluorescence quantum yields of 0.64, 0.29, 0.24, and 0.29, resp. In the case of 2 the detection limit of exciton coupling by FDCD is .apprx.200 pg/mL using a std. 1 cm fluorescence ***cell*** . Based on an equation described by I. Tinoco et al., the fluorescence detected CD spectra were converted into

conventional CD spectra with excellent agreement. The present examples of exciton coupling between 2 or 3 identical fluorophores demonstrate that FDCD provides a micro-scale tool for structural studies in which the

sensitivity is increased 50 to 100-fold relative to conventional CD under

favorable conditions. L20 ANSWER 35 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:621356 HCAPLUS

DOCUMENT NUMBER: 127:290382

Anaerobic degradation of cyclohexane-1,2-diol by a new TITLE:

Azoarcus species

AUTHOR(S): Harder, Jens

CORPORATE SOURCE: Max-Planck-Inst. Marine Mikrobiol., Bremen,

D-28359.

Germany

Archives of Microbiology (***1997***), 168(3), SOURCE:

199-204

CODEN: AMICCW; ISSN: 0302-8933

PUBLISHER: Springer DOCUMENT TYPE: Journal LANGUAGE: English

AB A bacterium, strain 22Lin, was isolated on cyclohexane-1,2-diol as sole electron donor and C source and NO3- as electron acceptor.

Cells

are motile rods and are facultatively anaerobic. A phylogenetic comparison based on the total 16S rRNA gene sequence allowed the assignment of the isolate to the genus Azoarcus. Cyclohexanol, cyclohexanone, cyclohexane-1,3-diol, and cyclohexane-1,3-dione, which are

oxidized by a different denitrifying strain, did not support denitrifying growth of isolate 22Lin. Cyclohexanol (150 = 37 .mu.M) and

cyclohexanone

(150 = 28 .mu.M) inhibited growth on cyclohexane-1,2-diol, but not on acetate. NAD was reduced by crude exts. of strain 22Lin in the presence of cyclohexane-1,2-dione, but not in the presence of cyclohexanone or cyclohexane-1,3-dione. The formation of 6-oxohexanoate from cyclohexane-1,2-dione and of adipate during NAD redn. suggests that

22Lin possesses a C-C hydrolase that transforms cyclohexane-1,2-dione to 6-oxohexanoate. This pathway was once obsd. in an aerobic pseudomonad

that was lost and could not be reisolated. Here, the application of strictly anoxic enrichment conditions enabled the reisolation of another strain (22Lin) that uses this pathway.

L20 ANSWER 36 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1997:342195 HCAPLUS

DOCUMENT NUMBER: 126:317567

Carbohydrate conjugates of piperidine and pyrrolidine TITLE:

derivatives as leukocyte adhesion inhibitors

INVENTOR(S): Toepfer, Alexander; Kretzschmar, Gerhard; Schoelkens,

Bernward; Klemm, Peter; Huels, Christoph; Seiffge,

Dirk

PATENT ASSIGNEE(S): Hoechst A .- G., Germany

Ger. Offen., 16 pp. SOURCE:

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE A1 19970410 DE 1995-19537334 19951009 <--DE 19537334 EP 787739 A1 19970806 EP 1996-115414 19960926 <--R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT. SE US 5739300 US 1996-726142 19961004 <--A 19980414 AU 1996-67997 19961007 <--AU 9667997 A1 19970417

APPLICATION NO. DATE

CN 1150155 19970521 CN 1996-113073 19961007 <--ZA 9608470 19970409 ZA 1996-8470 19961008 <---Α CA 1996-2187392 19961008 <--CA 2187392 AA 19970410 NO 9604268 19970410 NO 1996-4268 19961008 <--Α A2 19970428 JP 09110834 JP 1996-267002 19961008 <--BR 9605024 A 19980630 BR 1996-5024 19961008 <--PRIORITY APPLN. INFO.: DE 1995-19537334 A 19951009 MARPAT 126:317567

OTHER SOURCE(S):

/ Structure 3 in file .gra /

AB Conjugates of carboxylated piperidine or pyrrolidine derivs. linked to a pyranose, furanose or polyol via a linear or cyclic spacer were prepd. for use as selectin receptor antagonists. Thus, (1R,2R)-trans-1,2-***cyclohexanediol*** was treated with thioethyl 2,3,4-tri-O-benzyl-.beta.-L-fucopyranoside, followed by Et 4-piperidinecarboxylate, and debenzylation to give the glycoside 1. At 10 mg/kg i.v. in rats I caused 81% inhibition of leukocyte adhesion to blood vessel walls.

L20 ANSWER 37 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:71518 HCAPLUS

DOCUMENT NUMBER: 124:112247

TITLE: Stable antimicrobial dialdehyde composition and

methods of use

INVENTOR(S): Donovan, Daniel J.; Mcsherry, David D.; Fredell,

Dale

SE

PATENT ASSIGNEE(S): Ecolab Inc., USA

SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 887,312,

abandoned.

CODEN: USXXAM DOCUMENT TYPE: LANGUAGE: English FAMILY ACC, NUM, COUNT: 3 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 5480643 A 19960102 US 1993-65289 19930706 <--

US 1991-777782 19911016 <--US 5158778 A 19921027 WO 1994-US3688 19940331 <--Al 19950119 WO 9501724

W: AU, CA, JP, NZ

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,

AU 9471364 AU 1994-71364 19940331 <--Al 19950206 PRIORITY APPLN. INFO .: US 1991-777782 19911016

US 1992-887312 19920522 US 1993-65289 19930706 WO 1994-US3688 19940331

AB A stable, solid or semi-solid, antimicrobial compn. is provided

a dialdehyde antimicrobial agent such as glutaraldehyde, and a carbohydrate such as a sugar or a polyol such as a sugar alc. The compn. can be employed to ***preserve***, sanitize, disinfect, or sterilize a contaminated surface or area. The compn. can also be combined with an absorbing agent to produce a moisture absorbent antimicrobial compn. which

can be used to absorb and disinfect biol. spills such as body fluid

L20 ANSWER 38 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1995:761497 HCAPLUS

DOCUMENT NUMBER: 123:170190

TITLE: Preparation of monosaccharide or oligosaccharide derivatives containing fucose and/or (di)glutamic acid or lysine with specific binding affinity to adhesion

molecule ELAM-1

INVENTOR(S): Horie, Kazutoshi; Sakagami, Masahiro; Kuramochi,

Kentaro; Azuma, Kunio; Myoshi, Shiro; Yamada, Harutami

PATENT ASSIGNEE(S): Dds Kenkyusho Kk, Japan SOURCE: Jpn. Kokai Tokkyo Koho, 77 pp.

CODEN: JKXXAF DOCUMENT TYPE: Patent LANGUAGE: Japanese FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE -----

JP 06306092 A2 19941101 JP 1994-54562 19940228 <--PRIORITY APPLN. INFO.: JP 1993-63402 19930226

MARPAT 123:170190 OTHER SOURCE(S):

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. (1; F, Fi = monosaccharide selected from sialic acid, uronic acid, galactose, glucose, mannose, hexosamine, ribose, and rhamnose

or di- to tetrasaccharide consisting of these monosaccharides or their derivs.; n, m = 0-10; provided that when m = 0, Fi = H; T1, T2i = bond, NHCO, NHCO2, O2CNH, NHCONH, CONH, CO2, O2C, O; R1, R2, R3ai, R4ai, R5i, R6

= H, optionally amidated NH2, optionally etherified or esterified OH, optionally esterified or amidated CO2H, optionally amidated, etherified, or esterified C1-3 hydroxy- or aminoalkyl; i = 0, 1,2; or R6 and R1 or R3ai represents C1-4 n-alkylene or together with the bonded C-chain

a satd. 5- to 7-membered ring; I = 0-4; or R4ai, R5i = Q; wherein T3i, T4ij = group defined in T1; R10, R20, R30bij, R40bij, R50ij, R60 = group defined in R1 and R2; j = 0,1,2; p = 0-10; Fij = group defined in F; provided that when p = 0, Fij = H; at least one of F, Fi, and Fij = fucose or an oligosaccharide having fucose at the reducing terminus) are prepd. These compds. specifically bind to endothelial leukocyte adhesion mol. 1 (ELAM-1, selectin-1) expressed at inflammation sites of vascular endothelial ***cells*** , are useful in a drug delivery system which can efficiently and specifically deliver an antiinflammatory agent to the inflammation sites, and also may be used as ***cell*** recognition elements since they contain sugars such as fucose in the side chains. Thus, Boc-Glu-OH was treated with N-hydroxysuccinimide and DCC in MeCN at

room temp, for 4 h and condensed with 6-aminohexyl

2,3,4-tri-O-benzyl-L-

fucopyranoside p-toluenesulfonate to give, after hydrogenolysis over 10%Pd-C, a title compd. [II; R = Me3CO2C (Boc)] (III). III and II (R = Q1) at 10 mM in vitro competitively inhibited 50 and 80%, resp., (ELAM-1)-mediated intercellular adhesion between HL-60 ***cells***

and HUVEC ***cells*** on the surface of which ELAM-1 was induced by recombinant human interleukin-1.beta..

L20 ANSWER 39 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1994:456875 HCAPLUS

DOCUMENT NUMBER: 121:56875

TITLE: Dynamics of Five-Membered Rings in the Solid State by NMR Spectroscopy

AUTHOR(S): Lambert, Joseph B.; Johnson, Suzanne C.; Xue, Liang CORPORATE SOURCE: Department of Chemistry, Northwestern University,

Evanston, IL, 60208-3113, USA

SOURCE: J. Am. Chem. Soc. (***1994***), 116(14), 6167-74

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal LANGUAGE: English

AB The carbon-13 NMR spectra have been investigated in the solid state for

no. of fundamental five-membered rings and some analogous six-membered

rings. Several of these rings *** freeze*** into a plastic phase, whose NMR spectrum retains the symmetry of the liq.-phase spectrum.

the plastic-to-nonplastic transition, these spectra can undergo decoalescence to spectra characteristic of the symmetry and structure within the solid. Motion within the solid also broadens peaks when the motional frequency is comparable to the spin-lock precessional frequency. In the nonplastic phase, cyclopentanol exists in at least two sites, and possibly more, which probably result from hydrogen-bonded aggregation. Cyclohexanol may exist in two such sites. Cyclopentanone exists in two equally populated sites. 1-Methylcyclopentanol and trans-1,2-

cyclohexanediol exist either in two equally populated sites or as a single, unsym. form. Cyclohexanone, trans-1,2-cyclopentanediol, and tetrahydrothiophene 1-oxide appear to exist in single forms. Sulfolane exists in two, unequally populated sites.

L20 ANSWER 40 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:244153 HCAPLUS

DOCUMENT NUMBER: 120:244153

TITLE: Preparation of optically active cyclohexanediols and

(+)-.alpha.-hydroxycycloheptanone by an enzyme catalyzed stereoinversion/oxidation process

AUTHOR(S): Carnell, Andrew J.; Iacazio, Gilles; Roberts, Stanley

M.; Willetts, Andrew J. CORPORATE SOURCE:

Dep. Chem., Univ. Exeter, Exeter, EX4 4QD, UK

Tetrahedron Lett. (***1994***), 35(2), 331-4 SOURCE: CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 120:244153

/ Structure 4 in file .gra /

AB (.+-.)-Trans and cis Cyclohexane-1,2-diols undergo a double stereoinversion process to give trans-(S,S)-cyclohexane-1,2-diol on incubation with the fungus C. cassiicola. Treating substituted diols 1 (.alpha.-Me, .beta.-Me) under these conditions gave the corresponding diols Il without changing the Me config. Treating trans-1,2cycloheptanediol gave only cycloheptanone III.

L20 ANSWER 41 OF 54 HCAPLUS COPYRIGHT 2002 ACS 1994:86074 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

120:86074 TITLE: Conditioning shampoos containing anionic surfactant,

conditioning agents, and emulsifying agents INVENTOR(S): Bergmann, Wolfgang

PATENT ASSIGNEE(S): Helene Curtis, Inc., USA

Eur. Pat. Appl., 41 pp. SOURCE: CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ----------FP 566049 A1 19931020 EP 1993-105901 19930410 <--EP 566049 B1 19960724 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, US 5275761 A 19940104 US 1992-869538 19920415 <--

ZA 9301613 A 19931115 ZA 1993-1613 19930305 <--CA 1993-2092284 19930323 <--CA 2092284 AA 19931016 AU 9335503 A1 19931021 AU 1993-35503 19930324 <--AU 667515 B2 19960328 IL 105250 A1 19970610 IL 1993-105250 19930401 <--E 19960815 AT 140614 AT 1993-105901 19930410 <--ES 2090756 T3 19961016 ES 1993-105901 19930410 <--NO 9301375 A 19931018 NO 1993-1375 19930414 <--JP 06080539 A2 19940322 JP 1993-87585 19930414 <--JP 2559973 B2 19961204

US 5358667 A 19941025 US 1993-152251 19931112 <--

US 5456863 A 19951010 US 1994-278052 19940720 <--PRIORITY APPLN. INFO.: US 1992-869536 19920415 US 1992-869538 19920415 MARPAT 120:86074 OTHER SOURCE(S): AB Conditioning shampoos comprise (1) anionic cleansing surfactants such an alkyl ether sulfate and an alkyl sulfate, (2) water-insol. conditioning agents such as siloxanes and hydrocarbons, (3) emulsifying compns contg. polyhydric compds. and hydrophilic quaternary ammonium compds., (4) suspending agents, and (5) carriers. The compns. effectively resist phase sepn., clean the hair, and impart improved dry and wet stage conditioning properties to the hair in a single application. For example, a shampoo contained Na trideceth carboxylate 0.375, glycerin 3.00, dimethicone 4.125, ammonium lauryl sulfate 18.00, fatty alc. ether sulfosuccinate 4.00, Stabileze 06 0.40, citric acid 0.35, cocamide DEA 4.00, fragrance 0.40, ammonium xylene sulfonate 3.00, ***preservatives*** q.s., dyes q.s., and water to 100%. L20 ANSWER 42 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1990:530627 HCAPLUS 113:130627 DOCUMENT NUMBER: TITLE: Microbiological transformations 15. The enantioselective microbiological Baeyer-Villiger oxidation of alpha-substituted cyclopentanones AUTHOR(S): Alphand, Veronique; Archelas, Alain; Furstoss, Roland CORPORATE SOURCE: Lab. Chim. Org. Bioorg., Fac. Sci. Luminy, Marseille, 13288/9, Fr. SOURCE-Biocatalysis (***1990***), 3(1-2), 73-83 CODEN: BIOCED; ISSN: 0886-4454 DOCUMENT TYPE: Journal LANGUAGE: English AB Two strains of Acinetobacter were studied for enantioselective Baeyer-Villiger-type oxidn. of racemic .alpha.-substituted cyclopentanones. This allows a 1-step synthesis of various .delta.-lactones with optical purities of .ltoreq.97% using whole-***celi*** procedures. Tetraethylpyrophosphate and 1,2-***cyclohexanediol*** were used to enhance the yields. The obtained (S)-lactones are of high interest as readily accessible chirons as well as to the flavor industry. L20 ANSWER 43 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1990:457360 HCAPLUS DOCUMENT NUMBER: 113:57360 TITLE: Chemo-enzymic synthesis and characterization of L-tryptophan selectively 13C-enriched or hydroxylated in the six-membered ring using transformed Escherichia coli ***cells*** AUTHOR(S): Van den Berg, E. M. M.; Jansen, F. J. H. M.; De Goede, A. T. J. W.; Baldew, A. U.; Lugtenburg, J. CORPORATE SOURCE: Dep. Org. Chem., Leiden Univ., Leiden, 2300 RA, Neth. SOURCE: Recl. Trav. Chim. Pays-Bas (***1990***), 109(4), 287-97 CODEN: RTCPA3; ISSN: 0165-0513 DOCUMENT TYPE: Journal LANGUAGE: English OTHER SOURCE(S): CASREACT 113:57360 AB L-(3a-13C)- and L-(6-13C)tryptophan were synthesized from simple compds, via a single reaction scheme based on the conversion of 1.3-cyclohexanedione to indole. The labeled indoles were converted in 1

step to the corresponding L-tryptophans using transformed E. coli
cells with large amts. of tryptophan synthetase. The same

reaction scheme was used for the synthesis of 4- and 7-indolol. These

hydroxyindoles together with 5-indolol were converted to 4-, 7-, and

5-hydroxy-L-tryptophan, resp., using the E., coli ***cells*** . The

serotonin. 7-Indolol was the only indole deriv, converted faster than

L-tryptophans with a stable isotope (13C, 15N, or 2H) in the arom, ring

was completed. The NMR parameters of these monoisotopically labeled

unsubstituted indole by tryptophan synthetase. With the prepn. of

L-(3a-13C)- and L-(6-13C)tryptophan, the series of indoles and

systems are discussed.

latter compd. is the immediate precursor of the neurotransmitter

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INVENTOR(S):
                    Nomura, Hiroaki; Akimoto, Hiroshi; Miwa, Tetsuo
PATENT ASSIGNEE(S):
                        Takeda Chemical Industries, Ltd., Japan
SOURCE:
                  Eur. Pat. Appl., 35 pp.
             CODEN: EPXXDW
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                    English
FAMILY ACC, NUM, COUNT: 1
PATENT INFORMATION:
  PATENT NO.
                  KIND DATE
                                    APPLICATION NO. DATE
                                 EP 1989-303177 19890330 <--
  EP 340905
                A1 19891108
  EP 340905
                B1 19931208
     R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
  JP 02028162
                 A2 19900130
                                 JP 1989-28120 19890206 <--
  JP 2830008
                B2 19981202
                 A 19900807
  US 4946846
                                 US 1989-329374 19890327 <--
  AT 98244
                E 19931215
                                AT 1989-303177 19890330 <--
  DK 8901585
                     19891002
                                 DK 1989-1585 19890331 <--
                     19950116
  DK 169703
                 B١
  NO 8901369
                 Α
                     19891002
                                 NO 1989-1369 19890331 <--
  NO 169842
                 В
                    19920504
  NO 169842
                 C
                    19920812
  HU 51620
                 A2 19900528
                                 HU 1989-1614 19890331 <--
  HU 203102
                 В
                    19910528
  CN 1036567
                     19891025
                                 CN 1989-101906 19890401 <--
                 Α
  CN 1024007
                    19940316
                 В
  HU 210920
                 В
                    19950928
                                 HU 1990-8278 19901214 <--
  US 5223620
                     19930629
                                 US 1992-830884 19920204 <--
                                 JP 1988-82043
                                                  19880401
PRIORITY APPLN. INFO.:
                                     19890206
                     JP 1989-28120
                     US 1989-329374
                                       19890327
                     EP 1989-303177
                                       19890330
                     HU 1989-1614
                                      19890331
                     US 1990-521572
                                      19900510
OTHER SOURCE(S):
                        CASREACT 112:217539; MARPAT
112:217539
/ Structure 5 in file .gra /
AB The title compds. (I; A = optionally hydrogenated benzene or pyridine
  ring; R = glutamate residue; R1-R4 = H, F, alkyl; X = NH2, OH) were
prepd.
  Thus, R5CH2CH[CH(OMe)2](CH2)3C6H4(CO2CMe3)-4 [II; R5 =
CH(CN)2] (prepn.
  given) was cyclocondensed with (H2N)C:NH.HCl to give II (R5 =
   2,4,6-triaminopyrimidin-5-yl) which was stirred 18 h with CF3CO3H in
  CH2Cl2 and the product stirred 66 h with
H2NCH(CO2Et)CH2CH2CO2Et.HCl in
  DMF contg. (PhO)2P(O)N3 and Et3N to give, after sapon., the title
compd.
  III which had IC50 of <0.0025 and 10.0 .mu.g/mL for inhibition of
  thymidine uptake by HL-60 leukemia ***cells*** and for growth of
  embryonic lung fibroblast ***cells***, resp.
L20 ANSWER 45 OF 54 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                          1990:193544 HCAPLUS
DOCUMENT NUMBER:
                           112:193544
TITLE:
                In vitro studies of chemical effects on gap-junctional
             communciation: role of biotransformation in toxicant
             detection and use of assays in risk assessment
AUTHOR(S):
                    Malcolm, A. Russell; Mills, Lesley J.; Robson,
Deborah
CORPORATE SOURCE:
                          Environ. Res. Lab., Environ. Prot. Agency,
             Narragansett, RI, 02882, USA
                  In Vitro Toxicol. ( ***1990*** ), 3(1), 61-7
SOURCE:
             CODEN: IVTOE4; ISSN: 0888-319X
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L20 ANSWER 44 OF 54 HCAPLUS COPYRIGHT 2002 ACS

antitumor agents

112:217539

6-yl)propyl]benzoyl]glutamates and analogs as

1990-217539 HCAPLUS

Preparation of N-[4-[3-(2-aminopyrido[2,3-d]pyrimidin-

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:



DOCUMENT TYPE: LANGUAGE: English

AB Phenol, a weak promoter of mouse skin tumors, failed to inhibit gap-junctional communication between Chinese hamster V79 lung fibroblasts:

however, five metabolites of phenol suppressed gap-junctional communication in a concn.-related manner. Sodium cyclamate, a possible promoter of bladder cancer in rats, weakly inhibited gap-junctional communication in the same assay; however, its 3 metabolites were stronger

inhibitors than sodium cyclamate. Thus, some metabolic products may show

activity when parent compds. do not or may show greater activity than parent compds. The use of assays incapable of metabolizing test compds. permits distinction between parent compd. activity and that of metabolites tested sep. This may allow identification of groups at special risk because of differences in the metab. of parent compds. For example, humans and test animals capable of metabolizing cyclamate may be at

risk for tumor development than individuals without such capacity.

L20 ANSWER 46 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1984:583584 HCAPLUS

DOCUMENT NUMBER: 101:183584

Effect of DONU, a new water-soluble derivative of TITLE:

nitrosourea, on human tumors serially transplanted

into nude mice

AUTHOR(S): Asanuma, Fumiki; Kubota, Tetsuro; Hanatani, Yuji;

Tsuyuki, Ken; Nakada, Munehiko; Ishibiki, Kyuya; Abe, Osahiko

CORPORATE SOURCE:

Sch. Med., Keio Univ., Tokyo, Japan SOURCE: J. Jpn. Soc. Cancer Ther. (***1982***), 17(8),

2035-43

CODEN: NGCJAK; ISSN: 0021-4671

DOCUMENT TYPE: Journal LANGUAGE: Japanese

GI

/ Structure 6 in file .gra /

AB 2-((2-Chloroethyl)nitrosoamino)carbonylamino-1,3-***cyclohexanediol**

(DONU)(I) [92605-80-6] (10 mg/kg i.v.) caused marked regression of

undifferentiated breast carcinoma and poorly differentiated colon adenocarcinoma tumors transplanted in mice, but had no effect on other tumors (stomach cancer, cholangiocarcinoma, etc.). The sensitive adenocarcinoma tumors showed rapid disappearance of I when tumor ***tissue*** pharmacokinetics were examd. A correlation between

sensitivity to I and pharmacokinetics of I is suggested.

L20 ANSWER 47 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:175167 HCAPLUS

DOCUMENT NUMBER: 100:175167

TITLE: Microcalorimetric analysis of periodate-diols reactions in dilute aqueous solution. I. Outline of

methods and preliminary results

AUTHOR(S): Crescenzi, Vittorio; Gamini, Amelia; Cesaro, Attilio;

Delben, Franco; Paoletti, Sergio

CORPORATE SOURCE: Ist. Chim. Fis., Univ. Roma "La Sapienza",

Rome,

SOURCE: Gazz. Chim. Ital. (***1983***), 113(7-8), 387-92

CODEN: GCITA9; ISSN: 0016-5603

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The use of com. batch- and flow-type microcalorimeters, based on the heat-leakage twin- ***cells*** principle, for studying kinetic processes was investigated with two purposes. The first was to assess the reliability of calorimetric data in deriving rate consts. This point was confirmed by comparing the calorimetric data with those obtained for the same system by means of optical methods. The second goal was the study of

the kinetics and thermodn, of the reaction of periodate with vicinal diols in complex structures such as those of polysaccharides. The data

presented are limited to two preliminary examples of the application of microcalorimetry to the splitting reaction of trans-1,2-

cyclohexanediol and of carboxymethylamylose at low degrees of substitution, with the emphasis on the exptl. approach.

L20 ANSWER 48 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:48357 HCAPLUS

DOCUMENT NUMBER: 98:48357

TITLE: Microsomal 4-vinylcyclohexene monooxygenase and

mutagenic activity of metabolic intermediates

AUTHOR(S): Gervasi, P. G.; Abbondandolo, A.; Citti, L.; Turchi,

CORPORATE SOURCE: Ist. Mutagen. Differ., CNR, Pisa, 56100, Italy SOURCE: Ind. Environ. Xenobiotics, Proc. Int. Conf. (

1981), Meeting Date 1980, 205-10. Editor(s):

Gut, Ivan; Cikrt, Miroslav; Plaa, Gabriel L. Springer: Berlin, Fed. Rep. Ger.

CODEN: 48RKAL

DOCUMENT TYPE: Conference LANGUAGE: English

/ Structure 7 in file .gra /

AB The main 4-vinyl-I-cyclohexene (I) [100-40-3] metabolite formed in mice

liver microsomes after incubation for 10 min was 4-vinyleyclohexane-1.2diol (II) [31646-64-7]. Il attained max. concn. after I0 min. 4-vinyl-1,2-epoxycyclohexane (III) [106-86-5] showed max. formation

after 3 min of incubation. 4-vinyl-1-cyclohexene dioxide (IV) [106-87-6] was found only in trace amts. 4-ethyleneoxycyclohexane-I,2-diol (V) [45895-09-8] was not found but should be formed either from enzymic hydrolysis of IV or further 4-vinylcyclohexene monooxygenase [84084-10-6]

action on II. III and V were not mutagenic at different doses on Chinese hamster V-79 ***cells*** , but showed only cytotoxic effects up to 20 mM. On the contrary, IV was able to increase (.apprx.10 times) the forward mutation rate of V-79 ***cells*** . Since IV is found only in trace amts. [possibly because of its rapid hydrolysis to 4-(1,2-dihydroxyethyl)-1,2- ***cyclohexanediol***], there appears to be

L20 ANSWER 49 OF 54 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1969:488328 HCAPLUS

DOCUMENT NUMBER: 71:88328

TITLE: Side effects of reaction media in histochemical

blocking procedures

AUTHOR(S): Staple, P. H.

little or no mutagenic activity.

CORPORATE SOURCE: Sch. of Dent., State Univ. of New York,

Buffalo, N.

Y., USA

SOURCE: Histochem. J. (***1969***), I(4), 377-81

CODEN: HISJAE

DOCUMENT TYPE: Journal LANGUAGE: English

AB At some sites in rat abdominal skin and human gingiva, 0.2N NaOH, the reaction medium for I,2- ***cyclohexanedioI***, intensified the Sakaguchi reaction, staining with Pauly's reagent, and binding of anionic dye at pH 6.4. At other sites these reactions were reduced. At all sites in rat skin 0.2N NaOH slightly reduced staining after the ninhydrin-Schiff procedure. There were also alterations in staining with cationic dyes. Therefore, 0.2N NaOH may rupture linkages between polycationic

proteins and polyanions demonstrable by Alcian Blue. The blockade produced by acetic anhydride-pyridine mixts, was stable in the alk. conditions required for staining with Pauly's reagent. Pretreatment with pyridine alone reduced ***tissue*** binding of anionic dyes.

L20 ANSWER 50 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1969:103995 HCAPLUS

DOCUMENT NUMBER: 70:103995

Cryoprotectants for Crithidia fasciculata TITLE: stored at -20.deg.. Trypanosoma gambiense and T.

conorhini AUTHOR(S): O'Connell, Kathleen M.; Hutner, S. H.; Fromentin,

Huguette; Frank, Oscar; Baker, Herman CORPORATE SOURCE: Haskins Lab., New York, N. Y., USA J. Protozool. (***1968***), 15(4), 719-24 SOURCE: CODEN: IPROAR DOCUMENT TYPE: Journal LANGUAGE: English AB ***Cryoprotectants*** were tested in both complex and semidefined media for the trypanosomatid C. fasciculata. Near log-phase or end-of-log-phase cultures were frozen for 24-48 hrs. at .apprx. -20.degree., then warmed in air to room temp. Immediate motility was correlated with viability. The best protectant of the 83 tested was glycerol at .apprx.10% (wt./vol.). Survival without ***cryoprotectant*** was rare. Outstanding ***cryoprotectants*** (perhaps also useful solvents for drugs poorly sol. in water) were: ethylene glycol, diethylene glycol, 1,2,4-butanetriol, 1,4-***cyclohexanediol***, dimethyl sulfoxide, propylene glycol, N-acetylethanolamine. Several sugars were active, e.g., D-arabinose, sucrose, and sorbitol. Trypanosomes tolerated ***cryoprotectants*** much less; tolerance was better in growth media than in suspension media. T. gambiense was grown in blood-enriched media + 2-2.5% glycerol, suspended in 20% (wt./vol.) glycerol, then frozen; this permitted 3-week survival. T. conorhini survived 4 weeks after growth in media contg. glycerol 2.5% + ethylene glycol 4% + rutin 1.0 mg./ 100 ml. L20 ANSWER 51 OF 54 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1967:443383 HCAPLUS DOCUMENT NUMBER: 67:43383 TITLE: Synthesis of esters of .alpha.,.alpha.-dimethyl alkanoic acids AUTHOR(S): Zharova, E. Ya.; Puzitskii, K. V.; Rapoport, I. B.; Eidus, Ya. T.; Velizar'eva, N. I. SOURCE: Neftekhimiya (***1967***), 7(1), 92-6 CODEN: NEFTAH DOCUMENT TYPE: Journal LANGUAGE: Russian AB Neo acids (.alpha.,.alpha.-dimethyl acids) were prepd. by carboxylation olefins or monovalent satd, alcs, with CO at 40.degree./30-50 atm. in the presence of H2SO4. Homologs C13 (b17 165-200.degree.) and C16 (b10 165-98.degree.) were prepd. from tetramers or pentamers of propylene. Neo acids were then converted to the corresponding acid chlorides in 80-90% yield by adding excess SO2C12 dropwise at 76-9.degree.. The prepd. neo acids have the following b.p./mm., d20, and n20D: C5, 47-9.degree./10, 0.9676, 1.4312; C8, 57-8.degree./10, 0.9571, 1.4349; C9, 0.9497, -; C10, 90-1.5.degree/10, 0.9435, 1.4422; C11, 125-6.degree/21, 0.9347, 1.4443. Alcs. were acylated with acid chlorides at 50-100.degree., HCl was removed at 100.degree. with N, the products were washed with NaOH and Na2CO3 solns., then with water, and The yields were 85-95% with respect to acid chloride and 70-90% with respect to neo acid. Crude 1,3- ***cyclohexanediol*** esters contain monoesters and 65% diesters. Monoesters, ***freezing*** between -63 and -49.degree., have the following b.p. at 1-2 mm., n20D, and viscosity at 50.degree. in centistokes: C7, 105-68.degree., 1.4539, 8.2; C8, 120-80.degree., 1.4572, 6.4; C9, 135-92.degree., 1.4612, -; C10, 137-98.degree., 1.4608, 10.2; C11, 106-209.degree., 1.4612, 10.0. Analogously, the same values of diesters ***freezing*** between -46 and -40.degree. are as follows: C7, 168-70.degree., 1.4535, 9.5; C8, 180-1.degree., 1.4549, 11.2; C9, 192-4.degree., 1.4579, 15.9; C10, 198-200.degree., 1.4587, 21.8; C11, 209-11.degree., 1.4600, 24.4. These characteristics are further given for the esters of neo acids and polyols: C8, (CH2)6(OH)2 178-80.degree., 1.4430, 7.0; C7, (CH2)10(OH)2 192-4.degree., 1.4452, 8.6; C8, (CH2)10(OH)2 202-5.degree., 1.4481, 10.0; C7, trimethylolpropane, 213-24.degree., 1.4490-1.4509, 18.9-22.9. Diol esters ***freeze*** at the temp. between -63 and -69.degree., the triol ester at -45.degree.. The esters of 2-ethyl-1-hexanol and neo acids (***freezing*** at -67.degree, or lower) have the following characteristics (ordered in the above sequence): C7, 112-14.degree., 1.4330, 2.0; C9, 114-16.degree., 1.4365, 2.4; C13, 154-60.degree.,

5.7; C16, 156-66.degree., 1.4510, 7.0. Mixts. of esters of C7 neo acid and 2-ethyl-1-hexanol and 1,3- ***cyclohexanediol*** have improved

phys. properties. Thus, the mixt, of these esters in the ratio 1:4

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ACCESSION NUMBER:
                             1959:67568 HCAPLUS
DOCUMENT NUMBER:
                             53:67568
ORIGINAL REFERENCE NO.: 53:12232d-f
                 The order of addition of lithium to biphenyl
TITLE:
AUTHOR(S):
                     Egorov, Yu. P.; Kaplan, E. P.; Letina, Z. 1.;
              Shlyapochnikov, V. A.; Petrov, A. D.
CORPORATE SOURCE:
                            N. D. Zelinskii Inst. Org. Chem., Moscow
                    Zhur. Obshchei Khim. ( ***1958*** ), 28, 3258-62
SOURCE:
DOCUMENT TYPE:
                          Journal
LANGUAGE:
                       Unavailable
AB Examn, of ultraviolet and infrared spectra of 1-phenylcyclohexene (by
  dehydration of 1-phenylcyclohexanol with AcOH-H2SO4; b5 114.degree.,
  1.5679), 3-phenylcyclohexene (hydrogenation of hydroquinone over Ni in
  dimethylcyclohexane gave 1,4- ***cyclohexanediol***, which distd.
  HBr gave 1,4-dibromocyclohexane, which was chilled to ***freeze***
out
  the cis isomer, b5 80.degree., n20D 1.5408, which with PhMgBr gave the
  3-phenylcyclohexene, b4 85.degree., n20D 1.5370), phenyl-1,5-
  cyclohexadiene (by treatment of 53 g. 1-phenylcyclohexene with 55 g. Br2
  in Et2O 2 days; m. 54-55.degree.), phenylcyclohexane and the
  dihydrobiphenyl formed through the Li deriv. of Ph2 (to 40 g. Ph2 in 300
  ml. Et2O was added 4 g. Li and some glass beads; the whole was shaken
  hrs. and treated with EtOH yielding dihydrobiphenyl, b4 85-86.degree.,
  f.p. -5.degree, to -6.degree., n20D 1.5603, d20 0.9925) showed that the
  addn. of Li to Ph2 occurs not in the 1,4-positions (Schlenk, et al., C.A.
  22, 4493) but in the 3,6-positions. The typical spectra are reproduced.
L20 ANSWER 53 OF 54 HCAPLUS COPYRIGHT 2002 ACS
                             1948:2508 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                             42:2508
ORIGINAL REFERENCE NO.: 42:521b-c
TITLE:
                  The hydrogen bond. 11. Determination of configurations
              of some cis-trans isomers by means of
                 **cryoscopic*** data
                      Yuan, Han-ching
AUTHOR(S):
                    J. Chinese Chem. Soc. ( ***1947*** ), 15, 102-6
SOURCE:
DOCUMENT TYPE:
                          Journal
LANGUAGE:
                       Unavailable
AB cf. J. Chinese Chem. Soc. 7, 76(1940). ****Cryoscopic*** data on 2
   forms of .beta.-chlorocrotonic acid and on 2 forms of 1,2-
    ***cyclohexanediol*** have been obtained and applied to confirm the
  configurations of these substances. The results afford further examples
  of the application of H bond theory in stereochemistry.
L20 ANSWER 54 OF 54 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                             1932:208 HCAPLUS
DOCUMENT NUMBER:
                             26:208
ORIGINAL REFERENCE NO.: 26:13h-i,14a
TITLE:
                  X-ray investigation of certain derivatives of
              cyclohexane. V. alpha.- and .gamma.-1,2-
***Cyclohexanediol*** , .beta.-1,4-
***cyclohexanediol*** and .beta.-1,4-
                ***cyclohexanediol*** diacetate
AUTHOR(S):
                      White, T. N.
                    Z. Krist. ( ***1931*** ), 80, 5-17
SOURCE:
DOCUMENT TYPE:
                          Journal
LANGUAGE:
                       English
AB .alpha.-1,2- ***Cyclohexanediol*** is orthorhombic, with symmetry
  space group Vh15(D2hp.gamma..alpha..beta.). There are 8 mols.
  in the unit ***cell***, for which a = 7.62 A.U., b = 8.55 A. U. and c
  = 19.57 A. U , d25 = 1.182. .gamma.-1,2- ***Cyclohexanediol***
  (designated as the .gamma.-isomer because it does not agree with data
  concerning the .beta.-isomer) monoclinic prismatic, a:b:c: =
   1.954:1:0.716, .beta. = 103.9.degree., a = 19.13 A. U., b = 9.92 A. U., c.
  = 7.23 A. U., d24 = 1.147, 8 mols. in unit ***cell***, space group C2h6(C2hb.alpha.1). .beta.-1,4- ***Cyclohexanediol***, monoclinic
  prismatic, a:b:c = 0.293:1:0.339, .beta. = 96.degree., a = 6.32 A.U., b =
  21.2 A.U., c = 7.27 A. U., d20 = 1.18, 6 mols. in unit ***cell***,
  space group C2h5. .beta.-1,4- ***Cyclohexanediol*** diacetate,
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freezes at -63.degree. and has visocisity 6.06 centistokes at

L20 ANSWER 52 OF 54 HCAPLUS COPYRIGHT 2002 ACS

50.degree..

monoclinic prismatic, a:b:c = 2.344:1:1.168, .beta. = 107.4.degree., a = 13.56 A.U., b = 5.83 A.U., c = 6.72 A. U., d (approx.) 1.18, 2 mols. in unit ***cell***, space group C2h5.